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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 9 1961

PERITONEOSCOPY

ENDOSCOPIC REFINEMENT PAR EXCELLENCE

BY

RODOLFO HERRERA-LLERANDI, M.D., B.S., B.Ph.

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Endoscopic procedures are usually carried out by a specialist surgeon to diagnose the condition for which he will later carry out the indicated treatment. This is true of cystoscopy for the urologist, of bronchoscopy and oesophagoscopy for the thoracic surgeon, and of culdoscopy for the gynaecologist. When it comes to gastroscopy, the procedure may be carried out by a gastro-enterologist so as to save the patient from a needless surgical exploration: few gastroscopies are carried out by abdominal surgeons. Peritoneoscopy stands nevertheless by itself as the endoscopic procedure for which there is no decided assignment to surgeon or physician. As peritoneoscopy consists in examining the peritoneal cavity, it seems logical that the surgeon should be asked to do it; his constant meeting with gross intra-abdominal disease makes him more likely to diagnose correctly what he sees through the peritoneoscope; but although the physician, even if he specializes in gastro-enterology, is less likely to be so familiar with the inside of the abdomen, it is for him that peritoneoscopy is most useful, and his usual attitude of trying to keep patients away from surgery may enhance his enthusiasm for peritoneoscopy. The opposite occurs with the surgeon: he is usually impatient, and he may feel that a diagnosis is unsatisfactory when he cannot introduce his hands in the abdominal cavity to palpate the diseased organs.

These seem to be the reasons why peritoneoscopy has not been universally accepted. These are also the reasons why surgeons often criticize peritoneoscopy; but there is little doubt in my mind that the inconclusive findings, the complications, and the failures, which are frequently mentioned as criticisms of the procedure and as justification for the absence of a peritoneoscope in hospital, are in most cases explained on the basis of failure not of the method but of the one who carried out the procedure. When the technique is carefully and patiently followed, when the limitations, indications, and contraindications of the procedure are known, and when the endoscopist has acquired experience and enthusiasm, the results of peritoneoscopy will be most gratifying and will prove that the procedure has not only an academic but a truly practical interest.

Technique

The technique of the procedure is simple and varies little with the different instruments available to-day. The one with which we have experience is the peritoneoscope designed by Ruddock (1934). The patient is prepared as for a coeliotomy and placed in the dorsal decubitus position on a table which allows changes in position in the lateral and horizontal planes. After infiltration with 1% procaine locally, a 1.5 cm. incision is made in the midline transversely 2 cm. below the umbilicus. The subcutaneous fat is pushed away, an additional dose of procaine is infiltrated in the fascia and peritoneum, and a pneumoperitoneum is created with a small blunt trocar. When the abdomen is well distended (to the point of slight discomfort but not of pain for the patient) the blunt trocar is removed and the large trocar, with its sheath through which the peritoneoscope will be passed, is put in its place. During the introduction of both trocars it is useful to have the patient blow up his stomach so as to offer better resistance. It is also important to direct the trocar away from any known masses or previous incisions.

The trocar is removed from its sheath and the wide-vision telescope is introduced slowly, while looking through the objective, until it reaches the free space created by the pneumoperitoneum. The latter may require intermittent refilling and the lens of the telescope will usually become fogged up by condensation, but will clear up spontaneously (it may be warmed in hot water before being introduced, but hot saline should not be used because this will deposit crystals that will harm the lens).

Examination of the abdominal cavity must be systematic so as not to leave any area unexplored. We start to the right of the falciform ligament and follow the right lobe of the liver until the dome of the gall-bladder comes into view. The surface of the liver as well as the parietal peritoneum over it can then be examined as high up as the right diaphragm. By withdrawing the telescope and turning it approximately 340 degrees anti-clockwise and close to the parietal peritoneum the edge of the left lobe of the liver is seen. This is examined as was the right lobe, and underneath it can be seen the anterior wall of the stomach. The left diaphragm transmits the cardiac beat. The spleen is usually not seen unless it is enlarged; but occasionally, if the patient is rotated towards the right, its tip may come into view. If the examiner moves from the right to the left side of the patient he may then point the telescope towards the omentum and examine it carefully. While the patient is being placed in the Trendelenburg position the lower parietal peritoneum is observed as far as the pelvis, and loops of bowel come into view and are seen migrating towards the chest.

The pelvic structures can be examined best when the patient has reached the extreme Trendelenburg position. The iliac vessels can be followed and peristaltic waves can often be seen in the ureters. The urinary bladder, uterus, tubes, and ovaries can usually be seen, even though incompletely; but if the pelvic floor is rather deep, or there are adhesions, it is helpful to ask the assistant to do a rectovaginal examination so as to push up the pelvic organs towards the examining instrument. The sigmoid and caecum can be identified before the patient is straightened out once again. If the head of the table is raised beyond the horizontal position, the bowel and omentum fall back into the lower abdomen and it may be possible to see the gall-bladder and gastrohepatic ligament, which were previously hidden by omentum. The pancreas cannot be identified even in thin patients, but inferences may be drawn from any large mass in it (if there should be a bulge which raises either the stomach or the gastrohepatic or gastrocolic ligaments). The presence of recent pancreatitis may be diagnosed with certainty if there are nodules of fat necrosis (Herrera-Llerandi, 1945).

At the end of the examination a biopsy specimen can be taken either with the special biopsy forceps or with a needle. The former is introduced through the peritoneoscope sheath, together with its smaller-field telescope, and is used for obtaining specimens of omentum, peritoneal implants, or other nodules, and the instrument carries a cauterization connexion. The biopsy needle is used either in large tumours with carcinomatosis (where there is little danger of spreading the disease) or in the liver. We prefer needle to forceps for obtaining liver specimens not only because it gives a deeper sample but also because it is difficult to bite into the organ with the biopsy forceps without creating a rather large bleeding area. Before taking a specimen of the peritoneum, it is useful to infiltrate the area with procaine. The same thing is done before the introduction of the biopsy needle through the skin and abdominal wall. We usually prefer not to take a specimen of the spleen, although it has been done occasionally with impunity by others and by us, at the time of transparietal splenoportography (Herrera-Llerandi *et al.*, 1955). A Franseen needle has been used with satisfaction, although other modifications of the Iversen needle may be as good or better (Abrams, 1958; Menghini, 1958; *British Medical Journal*, 1959).

At the end of the procedure inspection is made of the biopsy site to make certain that it does not bleed and the instrument is removed. The pneumoperitoneum is allowed to escape as completely as possible and the skin is closed with one or two deep mattress sutures. The patient is then returned to the ward and allowed a full diet and bathroom amenities unless there are contra-indications to these.

It is occasionally useful, particularly in tuberculous peritonitis or carcinomatosis, to allow the omentum to herniate through the peritoneoscopy incision as the instrument is withdrawn, so as to obtain a large satisfactory biopsy specimen under direct vision and ligation. We have occasionally used a second trocar (from a thoracoscope) to obtain a specimen under guidance of the wide-angle peritoneoscope.

Coeliotomy affords a more complete method of exploration than peritoneoscopy: one can palpate instead of only seeing, and one can lift up and explore hidden or retroperitoneal structures. Peritoneoscopy, on the other hand, allows only a superficial visual exploration. But peritoneoscopy is almost entirely painless, it does not produce shock, it is short in duration, it is done under local anaesthesia, it requires minimal personnel and operating-room accessories, the stay in hospital need not be more than 36 hours, and mortality and morbidity are almost nil. Coeliotomy, on the other hand, is accompanied by post-operative pain and potential shock; and usually general anaesthesia and complete operating-room personnel and accessories are indispensable. The cost of abdominal exploration is ten times greater (Narancio *et al.*, 1945) than that of peritoneoscopy, and convalescence lasts several weeks after a stay in hospital for about one week. Mortality and morbidity are far from negligible—for example, an exploratory operation for inoperable cancer of the stomach is accompanied by a mortality that varies between 8 and 22%.

Indications

The following are the main indications for peritoneoscopy.

1. To establish a diagnosis of medical intra-abdominal disease which will not require surgical treatment—for example, portal cirrhosis.

2. To establish the aetiology in cases of hepatomegaly, splenomegaly, ascites, or jaundice which cannot be diagnosed satisfactorily using only clinical, radiological, and laboratory data—for example, portal hypertension.

3. To establish the presence or absence of an intra-abdominal tumour when this is not certain on the basis of physical and radiological examinations—for example, to distinguish between a follicular ovarian cyst and a small fibroid of the uterus.

4. To help in deciding the best approach to an intra-abdominal mass, and to decide whether this exploration is necessary; the presence of metastases is easy to establish usually, but the technical resectability of a tumour cannot be judged satisfactorily (Benedict, 1944a).

5. To establish the prognosis in a patient who refuses coeliotomy and to follow the progress of a patient under treatment for intra-abdominal disease. An example of this would be a patient with ascites from an inoperable ovarian carcinoma which has been treated with radioactive gold.

Other indications have been suggested by some authors who have tried to change peritoneoscopy from a diagnostic to a therapeutic procedure. Such is the case of feminine sterilization by electrocoagulation of the tubes (Anderson, 1937), of implantation of radium in an inoperable intra-abdominal tumour (Hope, 1937), or of aspiration of a large ovarian cyst (Benedict, 1944a). It has also been used in combination with hysterosalpingography (unpublished data) and with transvesicular cholangiography (Royer *et al.*, 1942). It is our feeling that on rare occasions one of these *tours de force* might prove useful and wise, but asking too much of peritoneoscopy will only lead to errors, disappointments, and a bad name for the classical procedure.

Dangers of Peritoneoscopy

No matter how enthusiastic one may become regarding peritoneoscopy, its limitations must be kept in mind, since it is not a complete abdominal exploration. The greatest danger is to forget this, and to deny the benefits of coeliotomy to someone who would profit from it. The other dangers are associated with its complications.

1. Subcutaneous emphysema will sometimes appear as a result of the patient's straining. It may also be caused by an incorrect position of the pneumoperi-

toneum needle. If this needle has not pierced the peritoneum it will give rise to a localized distension, which is easily recognized on the abdominal wall; this contrasts with the uniform tympanitic abdominal appearance after correct pneumoperitoneum.

2. Although I have described pain as minimal during peritoneoscopy, it must be remembered that the parietal peritoneum is very sensitive and the mere touching of it with the tip of the instrument will cause pain. The worse source of pain encountered was associated with the incomplete "rinsing out" of the instrument after it had been sterilized in the formaldehyde cabinet. It is most important to wash out the air bulb, and I usually blow some air from it gently towards my eyes before using it for the creation of the pneumoperitoneum.

3. Ascitic fluid may continue to escape through the peritoneoscopy incision after the procedure. This is, in cases of carcinomatosis, one of the causes of local malignant implants. These leaks are usually self-limited.

4. The peritoneoscopy wound may on rare occasions become infected. This is all the more likely in a teaching institution where the endoscopist allows observers to look through the instrument.

The above four complications are of little importance to the patient, but the next three must be regarded as serious.

5. Haemorrhage can present itself either as an immediate or as a late complication. It may be due to a biopsy, to hypoprothrombinaemia, or to trauma by the instrument. With regard to the biopsy, care must be taken, before removing the telescope, that no active bleeding is left behind. If there should be any, the use of electrocoagulation or of local pressure will be helpful: the latter, for example, can be used after needle biopsy of the liver if one presses the abdominal wall against the biopsy site after allowing the pneumoperitoneum to empty. Regarding improper prothrombin levels, it is paramount to have a near-normal prothrombin time before carrying out a peritoneoscopy. The possibility of trauma as a cause of haemorrhage can be due to "blind" use of the instrument without constant adequate observation through the telescope and represents a faulty technique; but it can also be due to the introduction of the instrument through a vascular channel in the abdominal wall: this presented itself in a patient with cirrhosis when the instrument was put through the midline above the umbilicus. Because of an enormous collateral venous channel which started bleeding profusely around the instrument, the incision had to be enlarged, and the bleeding was thus controlled without any ill effects. Since then we have always used the infra-umbilical incision for cases of portal hypertension.

6. Shock can present itself without haemorrhage. It may be a reaction to the premedication or to the local anaesthetic, or it may be the result of sudden intra-abdominal decompression in cases of massive ascites. We encountered this complication after the rapid evacuation of 12 litres of ascitic fluid in a patient with portal hypertension. Since then we have taken the precaution of emptying any large ascitic accumulations gradually in the course of the three or four days preceding peritoneoscopy; and if large volumes of fluid have been aspirated during peritoneoscopy, we apply local pressure to the abdomen for 24 hours after endoscopy without complete emptying of the pneumoperitoneum.

7. Perforation of a hollow viscus is probably the most severe complication of peritoneoscopy. According to Ruddock (1937), this happens in 1.6% of the cases. It usually occurs in patients with plastic peritonitis where intra-abdominal adhesions are responsible for the fixation of the viscus (Benedict, 1951). The most frequent site of perforation is the small bowel. This complication occurred once in our series of nearly 400 cases, and the perforation consisted of "tapping the gall-bladder" after introduction of the biopsy needle through the liver (see Case 2 below). Since that time we make it a point to take liver biopsies away from the level of the gall-bladder, the needle being directed diagonally upwards instead of vertically. The most important point about the complication of perforation is to realize what has occurred, and to carry out immediate coeliotomy without removing the endoscopic instrument. In another patient, because of the appearance of shock, the diagnosis of perforation with haemorrhage was made by a member of the resident staff, and a useless coeliotomy was carried out in the afternoon after peritoneoscopy. The shock in this patient was, as mentioned above, caused by the removal of ascitic fluid and would have been corrected by abdominal compression and vasopressors. Nevertheless, it seems better to carry out a needless exploration than to fail to explore the case that requires it.

8. One last complication of peritoneoscopy, even though not a true result of the endoscopic procedure, must be mentioned. It is associated with premedication: because routines are easily fallen into, one must guard against "the usual premedication" being given to a patient with myxoedema or cirrhosis. The following case will serve to illustrate this complication:

Case 1.—Mrs. X, aged 50, entered hospital because of painless jaundice and abdominal distension. She gave a history of radical mastectomy and *x*-ray therapy for cancer of the breast eight years previously. Her prothrombin time was normal and her chest *x*-ray film negative. Additional laboratory data and *x*-ray examination were postponed because it was felt that she had metastatic disease, and a peritoneoscopy was done to confirm it. So it did. During the entire procedure the patient was very sleepy, and in the course of the next 12 hours her sleep became progressively deeper until she died. Mediastinal and abdominal metastases were found at necropsy. The liver was almost entirely replaced by malignant implants. The cause of death was the premedication ordered by the resident, consisting of 15 mg. of morphine and 0.2 g. of pentobarbitone.

Review of Peritoneoscopy in 390 Cases

Of the peritoneoscopies carried out, the diagnosis was established in 286 (73.3%) and coeliotomy was avoided in 273 (70%). The failures were: missed diagnosis in 9 (2.3%) and complications in 11 (2.8%); there were two deaths. The various types of complication are shown in Table I. The diagnoses obtained by peritoneoscopy are shown in Table II.

The failures are probably the most important aspect of our experience to discuss. One of the two deaths (Case 1) was the result of erroneous premedication in a case of carcinomatosis. The other (Case 2) was due to perforation of the gall-bladder.

TABLE I.—*Complications Found in* 390 *Peritoneoscopies*

Wound sepsis	2 cases
Ascitic fluid leak	4 ,,
Excessive premedication	1 case (death)
Perforated viscus	1 ,, ,,
Reversible shock	2 cases
Local haemorrhage	1 case

TABLE II.—*Diagnosis in* 390 *Peritoneoscopies*

Peritoneoscopic Diagnosis	No. of Cases
Metatastic carcinoma	114
Cirrhosis	88
Normal abdominal cavity	55
Medical jaundice	27
Ovarian and uterine tumours	26
Surgical obstructive jaundice	18
Pelvic inflammatory pathology	14
Tuberculous peritonitis	12
Retroperitoneal tumour	11
Adhesive peritonitis	9
Fatty infiltration of liver	7
Procedure impossible	6
Hepatoma	1
Acute pancreatitis	1
Neuroblastoma	1

Case 2.—Mrs. Y, aged 65, presented with severe anaemia and a history of massive haematemesis and melaena. By *x*-ray and laboratory data the diagnosis of portal hypertension was probable, but the aetiology was not certain. At peritoneoscopy we found minimal ascites, a rough-looking liver, and a distended gall-bladder. A biopsy specimen of liver was taken with a Franseen needle, about 2 cm. above the liver edge, at the level of the gall-bladder bed, in a region where the liver surface had a whitish appearance, so as to rule out the possibility of a local metastasis. As soon as the aspirating syringe was used a gush of bile came into it. We decided to continue with the aspiration until the gall-bladder appeared collapsed and no bile could be obtained through the needle. When the needle was withdrawn no blood or bile was seen coming out of the "biopsy site." The patient was kept in bed and watched closely. She showed no unusual or unfavourable symptoms or signs during the course of the next 48 hours. Then she gradually became unconscious and distended. Several massive haematemeses occurred and she died rather suddenly on the third day after peritoneoscopy. Necropsy was not performed, but an abdominal paracentesis yielded bile-tinged ascitic fluid. Although the patient's physician blamed the gall-bladder aspiration for the death, it was our opinion that such was not the case, but that death was due to severe gastro-intestinal haemorrhages. Nevertheless, it cannot be denied that the erroneous aspiration of the gall-bladder was a complication of the peritoneoscopic procedure and a contributing cause of the patient's death.

Although pathological proof of the diagnosis was obtained in 73% of our patients, it must be pointed out that a much higher success would be shown if peritoneoscopy were not carried out for academic reasons, as was often the case in our series. The fact that in 70% of our patients coeliotomy was avoided is to us the best argument in favour of peritoneoscopy. It has been pointed out by others (Ruddock, 1934; Narancio *et al.*, 1945; Benedict, 1951) that the cost of a peritoneoscopy is one-tenth that of an exploratory coeliotomy without undesirable sequelae. If one adds to this saving in time and money the lessening of pain and suffering, there is little doubt that peritoneoscopy is a desirable humane procedure.

The variety of diagnoses established must be enlarged to include those reported by others (Ruddock, 1934; Benedict, 1944b, 1951): Boeck's sarcoid, arsenical hepatitis, haemachromatosis, ectopic pregnancy, lymphoma, von Gierke's disease, etc.

The following three cases are unusual enough to warrant short descriptions.

Case 3.—A man of 45 presented with severe epigastric pain. There was abdominal rigidity, but *x*-ray examination showed no free air under the diaphragm. He had no history of gall-bladder or ulcerative disease, but acute cholecystitis, acute pancreatitis, and perforated ulcer were regarded as good possibilities, and it was decided to carry out a peritoneoscopy. Uncountable pale yellowish implants were found on the parietal peritoneum and falciform ligament. One of these was taken for biopsy; the pathologist reported it as typical fat necrosis. The patient was treated conservatively and recovered satisfactorily.

Case 4.—A 3-year-old child was admitted to hospital because of dyspnoea and jaundice. Liver enlargement and fluid in the chest and abdomen were found on physical examination. A diagnosis of kwashiorkor with superimposed infectious hepatitis was made. In spite of his age and dyspnoea, a peritoneoscopy was carried out uneventfully. The liver was found to contain a greyish mass which contrasted with the colour of normal liver. A biopsy showed a neuroblastoma, and the child died from it after a gradual downhill course. At necropsy the peritoneoscopic diagnosis was confirmed. His tumour had spread and metastasized extensively.

Case 5.—A man aged 73 had previously had a diagnosis of cirrhosis established clinically and by liver biopsy. He had recently become emaciated, and his ascites did not respond to medical treatment. Instead of a repeat blind liver biopsy, we recommended peritoneoscopy, and this showed a discrete bulging in the right lobe of the liver close to the midline. Biopsy showed a typical hepatoma. The patient was discharged for terminal care.

Conclusions

We have found that peritoneoscopy fulfils a useful role in the diagnosis of intra-abdominal pathology. It is a simple, economical, essentially painless, and harmless procedure, but its usefulness and accuracy are in direct relation to the ability and experience of the peritoneoscopist. He should know its limitations, indications, contraindications, and dangers.

Because it is important to make macroscopic evaluations during the inspection of the abdominal cavity, it seems logical to recommend that peritoneoscopies be carried out by an active abdominal surgeon, but it is indispensable that he should have the correct attitude regarding this procedure: he must be wise and avoid conclusions without solid proof (which might deprive a patient of a desirable coeliotomy); he must be patient, adroit, and anxious to save the patient from a fruitless abdominal exploration. A physician will usually have the correct philosophy regarding the procedure, but he may lack the useful experience of daily intra-abdominal inspection.

It is our experience that the pathological study of the liver is more accurate and satisfactory when a needle aspiration biopsy is carried out under peritoneoscopic guidance than with the standard bite biopsy and electrocoagulation instrument.

Except in very rare instances, peritoneoscopy should not be carried out in uncooperative patients (this includes children and psychoneurotic adults); nor should it be carried out on patients *in extremis*, in cases of peritonitis, in the presence of hypoprothrombinaemia, or of obliteration of the abdominal cavity by adhesions.

An experienced peritoneoscopist will prove to be a most important member of the hospital staff. His useful contributions will cause him to be regarded by physicians and surgeons as the endoscopist *par excellence*.

Summary

The experiences with peritoneoscopy in 390 cases are presented.

The benefits to the patient and to the hospital have proved the usefulness of peritoneoscopy for the establishment of certain intra-abdominal diagnoses without exploratory coeliotomy.

The information obtained by the endoscopist depends directly on his experience, and his knowledge of the limitations, indications, and contraindications of peritoneoscopy.

For the evaluation of hepatic disease we prefer needle aspiration biopsy under peritoneoscopic guidance to biopsy with biting forceps and electrocoagulation.

A hospital is considered to be not completely equipped if it lacks a peritoneoscope and a peritoneoscopist.

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TUBELESS GASTRIC ANALYSIS WITH AZURE A AND BETAZOLE HYDROCHLORIDE

BY

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The ability of the stomach to secrete hydrochloric acid (Prout, 1824) is often a crucial observation in the differential diagnosis of diseases affecting the alimentary tract. In an attempt to overcome the unpleasant necessity for intubation, Segal *et al.* (1950a, 1950b) introduced the method of "tubeless gastric analysis" which depends on the dissociation of a cation exchange resin by the hydrochloric acid in the stomach. This cation is absorbed and appears in the urine, where it is simple to estimate the quantity of cation excreted.

The first exchange resin used contained quininium ("diagnex"), which requires an ether–sulphuric-acid extraction of the urine and is thus rather inconvenient for routine use. More satisfactory is the dye azure A, which is present in considerable quantities in commercially available methylene blue (Segal *et al.*, 1955). This is used in diagnex blue ("azuresin"). Dilute hydrochloric acid displaces the dye from its carbacrylic exchange resin "amberlite RXE-96," and examination of the urine in a comparator block indicates the quantity of the dye excreted, release of which both *in vivo* and *in vitro* starts at *p*H 3.2 and is maximal at *p*H 1.5. Segal *et al.* (1950a, 1950b, 1955) had used 500 mg. of caffeine benzoate as parietal-cell stimulant, but after the successful clinical trials by Kirsner and Ford (1955) of the histamine isomer betazole hydrochloride [3-(2-β-aminoethyl) pyrazole] ("histalog") as gastric stimulant, Segal *et al.* (1959a, 1959b) replaced the caffeine with 50 mg. of betazole hydrochloride given orally or subcutaneously.

We are now in agreement with the extensive American experience which suggests that the azure A test combined with betazole hydrochloride is a useful and reliable procedure for indicating the presence of acid in the stomach and deserves wider clinical application. In this paper we record our further experiences with this test, which we use routinely in screening patients for achlorhydria. In many instances the results of the tubeless analyses were confirmed by comparison with the augmented histamine test of Kay (1953).

Present Study

Selection of Patients.—We studied 182 patients, of whom 50 were out-patients. A high incidence of achlorhydria was expected, for most of the patients selected suffered from diseases thought to be more commonly associated with achlorhydria, such as pernicious anaemia, iron-deficiency anaemia, rheumatoid arthritis, thyrotoxicosis, myxoedema, and polycythaemia vera.

Test Procedure.—This was essentially the same as that reported earlier from this department (Denborough *et al.*, 1958). After an overnight fast the bladder was emptied, the urine was discarded, and the patients were given either 500 mg. of caffeine or 50 mg. of betazole hydrochloride diluted in a glass of water. One hour later the bladder was emptied again and the "control" specimens were collected. Immediately afterwards 2 g. of the granules containing the dye azure A were given by mouth and the patients instructed not to have anything else until two hours later, when the bladder was emptied and the "test" specimens were obtained.

Method of Estimation.—Like Gilbert *et al.* (1957), we accepted as indicating the presence of acid only those tests in which the colour of the urine matched or was darker than the 0.6-mg. standard; less colour indicated achlorhydria. It was found that the estimation could be simplified in two ways without lowering the accuracy of the interpretation. Dilution of the urine specimens to 300 ml. was not necessary. Instead of heating aliquots suspected of containing reduced dye in a water-bath for 10 minutes, the specimens, to which one drop of Benedict's reagent and one drop of 6 N hydrochloric acid had been added, were heated gently over an open flame until the maximum colour had developed. They were then cooled under running water and compared with the standards supplied by the manufacturers.

Test of Comparison.—The results of the tubeless tests were correlated with the augmented histamine test carried out in the manner described by Kay (1953), but we used only 50 mg. of mepyramine maleate as the antihistamine and we collected specimens for one hour after the injection of histamine. Titration was carried out with decinormal NaOH to *p*H 7.4 in a direct-reading *p*H meter, and the results were expressed as the total milli-equivalents of acid secreted in one hour (mEq/hr.) after the injection of histamine (Bock, 1961a). The normal range for men would appear to be 15–30 mEq/hr. (mean 22.4 mEq/hr.) and for women about 5 mEq/hr. less (mean 14.6 mEq/hr.) (Bruce *et al.*, 1959).

Results

In the 77 subjects given caffeine as gastric stimulant the azure A test indicated the presence of acid (positive result) in 51 and apparent achlorhydria (negative result) in the other 26 (Table I). None of the positive results

was checked by intubation and 9 of the negative results were not checked. Of the remaining 17 patients with apparent achlorhydria 11 were found to secrete acid on augmented histamine stimulation and in five this was in excess of 11 mEq/hr.

TABLE I.—*Comparison of Azure A Results With Augmented Histamine Tests (A.H.T.)*

Stimulant	Total	Azure A Results	No.	A.H.T. Result		Not Checked
				Acid	No. Acid	
Caffeine	77	Acid	51	—	—	51
		No Acid	26	11	6	9
Betazole hydrochloride	105	Acid	68	27	2	39
		No Acid	37	3	18	16
Total ..	182		182	41	26	115

Betazole hydrochloride was used as a stimulant in 105 patients and acid was detected in 68. The augmented histamine test was carried out in 29 of the 68 patients and the presence of acid was confirmed in 27. Seven of them secreted 5 mEq/hr. or less, the lowest amount being 1.21 mEq/hr. This group included three patients with megaloblastic anaemia who had been referred to this department with achlorhydria, which had been established by "routine fractional analyses"; in each case acid was secreted in response to augmented histamine stimulation. Two false-positive results using betazole hydrochloride were noted in this series. In both, subsequent inquiry revealed that collection of the test specimens had been delayed. Repeat tests, which included collections at the same intervals as in the first test, showed very little dye in the urine at the correct time but sufficient colour in the subsequent specimens to warrant classifying them as positive.

Of 21 patients whose azure A tests after betazole hydrochloride were negative, augmented histamine stimulation revealed achlorhydria in 18; the other three secreted 0.21, 2.01, and 8.0 mEq/hr. respectively. This comparison was not undertaken in the remaining 16 cases of apparent achlorhydria. Betazole hydrochloride was a better stimulant than caffeine benzoate, since acid was detected in only three of the 21 negative tests when this drug was used, whereas 11 of the 17 patients in whom achlorhydria was suspected after caffeine benzoate secreted acid. Betazole hydrochloride was also a safe drug to use; only twice were unpleasant side-effects noted in the 105 tests. A 45-year-old woman developed a generalized urticarial eruption which responded to an antihistamine preparation, while an 18-year-old girl vomited. A few patients complained of mild headache.

Discussion

A review of the available literature indicates that 146 false-negative results (7.1%) and only 27 false-positive results (1.3%) were detected in 2,054 tubeless analyses which were checked by gastric intubation (Table II) (Segal *et al.*, 1950b, 1955; Malach and Banks, 1952; Becker and Maslon, 1953; Conway and Meikle, 1953; Flood *et al.*, 1953; Harkness and Durant, 1953; Sharp *et al.*, 1954; Shay *et al.*, 1954; Pollard *et al.*, 1954; Fentress and Sandweiss, 1955, 1957; Galambos and Kirsner, 1955; Goldbloom *et al.*, 1955; Segal and Miller, 1955; Sievers and Gieselman, 1956; Bolt *et al.*, 1957; Gilbert *et al.*, 1957; Poliner *et al.*, 1957; Rechtshaffen *et al.*, 1957; Sievers and Fischer, 1957; Denborough *et al.*, 1958; Rodman *et al.*, 1958; Rosenthal and Buscaglia, 1958; Glass *et al.*, 1960; Marks and Shay, 1960.

TABLE II.—*Comparison of Tubeless Analyses With Findings on Intubation*

Indicator Used	Tubeless Result	Intubation Result		Total	Total Checked
		Acid	No Acid		
Quininium	Acid	476	11	487	682
	No Acid	18	177	195	
Azure A	Acid	831	16	847	1,372
	No Acid	128	397	525	
Total ..		1,453	601	2,054	2,054

Although more false-negative results occurred with azure A, 9.4%, against 2.2% using quininium, some of this difference may be accounted for by the better techniques used for comparison in the azure A studies. Betazole hydrochloride is a better stimulant than caffeine benzoate, since acid was detected after betazole hydrochloride stimulation in 51% of 149 patients in whom caffeine indicated achlorhydria (Segal *et al.*, 1959b). We did not attempt to evaluate the azure A–betazole hydrochloride test as a possible method for the quantitative assessment of acid secretion, but we found no false-negative results among those patients who secreted 10 mEq/hr. or more after augmented histamine stimulation. This suggests that a negative azure A–betazole hydrochloride test would be strong evidence against the diagnosis of duodenal ulceration (Marks and Shay, 1960).

Intubation is uncomfortable and, particularly in older people, often difficult or impossible. Unless the tube is screened and its position localized in the stomach, the tip, according to Callender *et al.* (1960), can be in the pharynx, oesophagus, fundus of the stomach, or duodenum in 44% of cases. The reaction of the gastric juice can be alkaline because the unpleasant psychological influences consequent upon the anticipation and passing of the tube have inhibited acid secretion (Grossman *et al.*, 1945; Wolf, 1959). Some patients who secreted less than normal amounts of acid on augmented histamine stimulation, but in whom azure A–betazole hydrochloride tests were positive, had no detectable acid in the basal secretion (Bock, 1961b). The augmented histamine test is a somewhat arduous procedure. The tubeless method of gastric analysis overcomes these difficulties at the expense of a small proportion of false-negative results.

The azure A–betazole hydrochloride method of analysis is not infallible as a screening test for the detection of acid in the stomach. In such a screening test false-negative results are not a source of anxiety provided they are not too frequent, as negative results will usually be confirmed by intubation of the stomach. False-positive results are a good deal more worrying, as they denote a failure in the screening procedure. Although false-positive results are possible, they appear to be extremely infrequent when the test is properly performed. Interpretation of the test should be cautious in patients who have pyloric stenosis, malabsorption syndrome, severe diarrhoea, or renal disease (Poliner *et al.*, 1957; Bolt *et al.*, 1957; Rodman *et al.*, 1958).

Summary

The results of 182 tubeless gastric analyses using the dye azure A (diagnex blue) as indicator are reported. In 105 of these tests 50 mg. of betazole hydrochloride ("histalog") was used as the stimulant instead of 500 mg. of caffeine benzoate.

In 67 instances the results of the tubeless test were compared with the findings after augmented histamine stimulation. Only two false-positive results were detected, and these were explained by errors in technique. Fewer false-negative results occurred with betazole hydrochloride than when caffeine benzoate was used as the stimulant.

The tubeless method of gastric analysis, using the dye azure A and betazole hydrochloride, appears to be a reliable method for the screening of patients for achlorhydria.

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A new £75,000 training centre for rural medical aids in Tanganyika was formally opened at Ifakara on July 22. The centre is staffed by three doctors, two biologists, and three technicians, and is sponsored and financed by a Swiss organization, the Basle Foundation for Aid to Developing Countries.

FAECAL P.V.P. EXCRETION IN HYPOALBUMINAEMIA AND GASTRO-INTESTINAL DISEASE

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Until recently hypoproteinaemia in disease has been ascribed to poor intake, impaired absorption, or faulty metabolism of such protein precursors as amino-acids or peptides. Apart from the nephrotic syndrome, excessive catabolism or loss from the body has only rarely been invoked. Nevertheless recent reports indicate that excessive catabolism due to loss of protein into the intestinal tract is predominant in a variety of disorders associated with low serum proteins (Citrin *et al.*, 1957; Gordon, 1959a; Schwartz and Jarnum; 1959; Steinfeld *et al.*, 1960; Jarnum and Schwartz, 1960). Hypoproteinaemia results because the liver has only a limited capacity to synthesize albumin, and breakdown soon outstrips synthesis (Schwartz and Jarnum, 1959; Steinfeld *et al.*, 1960).

Intestinal loss is difficult to demonstrate because the gut lumen is relatively inaccessible and any exuded protein is broken down by digestive enzymes and the products are reabsorbed so that the faecal nitrogen is not necessarily raised. Similarly, if plasma albumin labelled with ^{131}I is used as a tracer, it enters the gut lumen, is broken down and the radioactive products are reabsorbed, and the faecal radioactivity may be normal. The ingenious technique of Gordon (1959a) of using polyvinylpyrrolidone (P.V.P.) has partially overcome the problem. P.V.P. labelled with ^{131}I is of similar molecular size to albumin, and so, when injected intravenously, can leak through sites that are permeable to the albumin molecule. In contrast to albumin it is relatively unchanged by the action of digestive enzymes and colon bacteria, and therefore much of it can reach the faeces, where it can be assayed by counting the radioactivity of the iodine label. This paper reports the results of this test obtained in a group of patients with a variety of disorders associated with hypoproteinaemia.

Methods

The P.V.P., which was obtained from May and Baker Limited, had an average molecular weight of about 40,000. It was labelled with ^{131}I as described by Gordon (1958) and dialysed in a Visking tube against running water to constant activity. This usually took three days. The starting polymer was slightly different from that used by Gordon and the product probably resembled that produced by Ravin *et al.* (1952). When fed by mouth approximately 40% was recovered in the faeces, less being recovered if the patient was constipated or the preparation was old. Even so, this preparation has proved to be satisfactory for the intravenous test when used within one week of preparation. The material was

autoclaved before intravenous use, and this was shown not to cause any liberation of free iodine. After blocking the patient's thyroid with potassium iodide, 10–20 μc of ^{131}I P.V.P. was given intravenously and the urine and faeces were collected separately for four 24-hour periods, care being taken to prevent urine contamination of the faecal specimen. The radioactivity of the specimens was measured in a circular ring counter containing eight Geiger tubes. The results are expressed as the percentage excretion in the faeces of an intravenous dose in a four-day period. The serum albumin was measured during this period by electrophoresis and scanning.

Twenty-one patients with a variety of gastro-intestinal disorders were studied (Tables I and II). These included giant rugal hypertrophy of the stomach, idiopathic steatorrhoea (proved by small-intestinal biopsy), ulcerative lesions of the gut, and idiopathic hypoproteinaemia. One of the cases (No. 16) of idiopathic hypoproteinaemia has previously been reported by Bound and Hackett (1953). The two patients labelled cryptogenic steatorrhoea failed to show any of the known causes for the steatorrhoea either in life or finally at necropsy. Eleven of the patients had a low serum albumin level (<3.5 g./100 ml.). The test was also performed on five patients with cirrhosis of the liver and two with the nephrotic syndrome (Table III). Eighteen patients without disorders of protein metabolism or disease of the gastro-intestinal tract were also studied.

TABLE I.—*^{131}I-P.V.P. Excretion in Patients with Gastro-intestinal Disease and Idiopathic Hypoproteinaemia*

Case No.	Age and Sex	Diagnosis	Serum Albumin (g./100 ml.)	Faecal ^{131}I P.V.P. (% I.V. Dose)	Faecal Fat g./24 hr.	Remarks
1	43 M	Giant rugal hypertrophy of stomach	3·7 4·3	2·6 0·4		Albumin half-life 17 days (normal 20–25 days) After subtotal gastrectomy
2	53 F	Idiopathic steatorrhoea	3·3 4·8	9·7 0·5	9 1	Gluten-free diet
3	73 F	,, ,,	4·0	1·0	2·4	
4	62 M	,, ,,	4·2	1·4		
5	42 F	,, ,,	3·8	0·5	8·8	
6	53 F	Cryptogenic steatorrhea	2·1	7·1	18	? Post-irradiation
7	42 M	,, ,,	4·6	2·5	10·7	Carcinoma of bronchus associated with hyponatraemia
8	69 M	Jejunal diverticulosis	4·0	2·7	25	
9	60 F	,, ,,	4·2	0·8	2·5	
10	53 F	Biliary-enteric fistulae	2·3	4·9		
11	56 M	Amyloidosis	3·7	3·7		Secondary to rheumatoid arthritis
12	51 M	Pancreatic steatorrhea	3·7	1·1	21·5	
13	55 M	Total gastrectomy	2·3	0·9		Gross diarrhoea and malnutrition
14	65 F	Systemic sclerosis	3·7	0·9	2·6	Involvement of oesophagus and gut
15	56 F	Idiopathic hypoproteinaemia	2·6 3·3	10·3 2·7		
16	8 M	,, ,,	1·8	5·4		

TABLE II.—*^{131}I-P.V.P. Excretion in Patients with Ulcerative Disease of the Bowel*

Case No.	Age and Sex	Diagnosis	Serum Albumin (g./100 ml.)	Faecal ^{131}I P.V.P. (% I.V. Dose)	Remarks
17	67 M	Ulcerative jejunitis	1·4	20·7	Gross diarrhoea
18	49 M	Ileitis	2·4	13·4	
19	38 F	Regional ileitis	2·2	3·6	Active
			3·4	0·1	Quiescent
20	16 M	Cirrhosis and ulcerative colitis	3·5	0·05	Pre-colitis
			2·4	3·4	Active colitis
			4·2	0·4	Quiescent
21	26 M	Ulcerative colitis	2·8	3·4	Active
			4·2	0·5	Quiescent

TABLE III.—*Faecal ^{131}I-P.V.P. Excretion in Patients with Hepatic Cirrhosis and the Nephrotic Syndrome*

Case No.	Age and Sex	Diagnosis	Serum Albumin (g./100 ml.	Faecal ^{131}I P.V.P. (% I.V. Dose)	
22	41 F	Cirrhosis	1·9	0·7	Diarrhoea. Faecal fat 19 g./24 hr.
			2·0	0·1	No diarrhoea
23	60 M	,,	2·4	0·1	
24	63 F	,,	4·3	0·1	Diarrhoea
25	73 M	Intrahepatic bile-duct carcinoma	2·6	0·1	
26	60 M	Primary biliary cirrhosis	4·0	0·1	
27	36 F	Nephrotic syndrome	2·2	1·0	
28	38 F	,, ,,	3·1	0·1	

Results

Patients who had neither disorders of protein metabolism nor disease of the gastro-intestinal tract had a mean four-day faecal excretion of intravenous ^{131}I P.V.P. of 0.52%, with a range of <0.05–1.6%. This has been taken as our normal range. We have confirmed Gordon's (1959a) observation that hypoproteinaemia *per se* does not give a false-positive result, for three patients with hepatic cirrhosis and two with a nephrotic syndrome, all with hypoalbuminaemia, had a normal excretion of ^{131}I P.V.P. (Table III). Similarly diarrhoea or steatorrhoea alone does not cause a false-positive result, as one patient with diarrhoea (Case 24) and four with gross steatorrhoea and diarrhoea (Cases 5, 12, 13, and 22) had a normal P.V.P. excretion.

In patients with gastro-intestinal disease and idiopathic hypoproteinaemia (Tables I and II) there is a roughly hyperbolic relationship between the serum albumin level and the faecal ^{131}I P.V.P. excretion (Fig. 1), similar to that described by Gordon (1959b). All but one of the patients with hypoproteinaemia had a high faecal excretion of ^{131}I P.V.P. As this patient (Case 13) had had a total gastrectomy for recurrent peptic ulceration, it is probable that this man's hypoproteinaemia could be accounted for by a poor appetite coupled with gross malabsorption. Four of the 15 tests on patients with a normal serum albumin level were abnormal, but three of these patients had a serum albumin level at the lower limit of normal—that is, 3.5–4 g./100 ml. These four patients suffered from amyloidosis associated with rheumatoid arthritis (Case 11), giant rugal hypertrophy of the stomach (Case 1), jejunal diverticulosis (Case 8), and cryptogenic steatorrhoea (Case 7). Such an overlap is not surprising, for

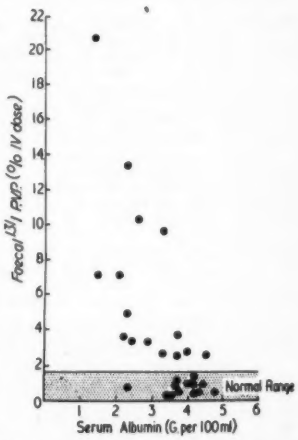

FIG. 1.—Relationship between serum albumin and ^{131}I-P.V.P. excretion in patients with gastro-intestinal disease or "idiopathic" hypoproteinaemia. The stippled area represents normal range of excretion of ^{131}I P.V.P. (Reproduced by courtesy of the Honorary Editors of the *Proceedings of the Royal Society of Medicine*.)

a diminished total body albumin may not initially be reflected by a low serum albumin level; also, the loss from the gut may fluctuate.

Serial Studies

Six of the patients with an abnormal ^{131}I-P.V.P. excretion were studied more than once (Tables I and II) and cases histories of three of these are described.

Case 1. Giant Rugal Hypertrophy of the Stomach (effect of subtotal gastrectomy).—A 43-year-old man had complained of epigastric pain for four years. A barium meal initially showed rather coarse rugae but within normal limits. During the last six months pain had increased and had caused loss of time from work. A further barium meal in July, 1960 (Fig. 2), showed grossly hypertrophic rugae in the stomach and this finding was confirmed by gastroscopy. There was no history of oedema, and the serum albumin was 3.7 g./100 ml. The ^{131}I P.V.P. test showed a raised faecal excretion (2.6%), while an albumin turnover showed a slightly shortened half-life of 17 days (normal 20–25 days). A subtotal gastrectomy was performed in August, 1960, and the diagnosis of giant rugal hypertrophy of the stomach was confirmed (Fig. 3). The operation brought relief of the abdominal pain, the serum albumin rose to 4.3 g./100 ml., and the faecal excretion of ^{131}I P.V.P. became normal (0.4%).

Case 2. Idiopathic Steatorrhoea (effect of a gluten-free diet).—This patient, a 53-year-old woman, had had diarrhoea for the 18 months preceding admission in November, 1959. Her bowels were open five or six times a day and the stools were loose, pale, and offensive. She was underweight (42 kg., later dropping to 37 kg.), with marked pitting oedema of the ankles. Investigation showed the typical picture of a malabsorption syndrome with an iron-deficiency anaemia, hypoproteinaemia (serum albumin 3.3 g./100 ml.) and steatorrhoea (faecal fat 9 g./24 hours). The absorption of folic acid, vitamin B_{12} and xylose was impaired. A jejunal biopsy showed complete "atrophy" of the villi, and the P.V.P. excretion over a three-day period totalled 9.7% of the administered dose. She was treated with a gluten-free diet, and over the next few months improved dramatically. By October, 1960, she had gained 12 kg. and passed only one normal motion daily. The serum albumin had risen to 4.8 g./100 ml. and the faecal fat excretion was less than 1 g. a day. The total ^{131}I-P.V.P. excretion over a four-day period was normal (0.5%).

FIG. 2.—Case 1. Barium-meal radiograph of patient with giant rugal hypertrophy of the stomach.

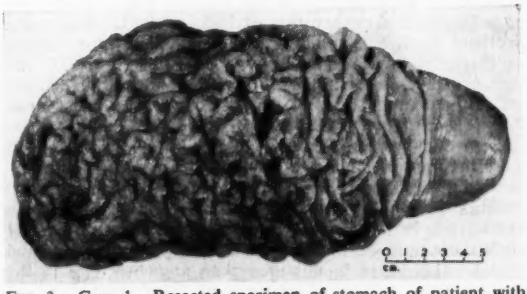

FIG. 3.—Case 1. Resected specimen of stomach of patient with giant rugal hypertrophy.

Case 15. Idiopathic Hypoproteinaemia.—A 56-year-old woman had complained of ankle oedema for three years, with tiredness, fluctuant diarrhoea, and, on some occasions, rectal bleeding. In June, 1959, she was investigated by Dr. Wade Volwiler, in Seattle, when radiographs of her gut and sigmoidoscopy were normal. At that time her serum albumin level was 2.6 g./100 ml. and the ^{131}I-P.V.P. excretion 10.3% (occult blood being absent at this time). While in London during May, 1960, her symptoms had diminished, her oedema was mild, her serum albumin level had risen to 3.3 g./100 ml., and the ^{131}I-P.V.P. excretion in her faeces was 2.7%. Her symptoms still fluctuated, and whether she will remain a patient with "idiopathic hypoproteinaemia" or whether frank gastro-intestinal disease will declare itself is unknown.

Ulcerative Lesions of the Gut

The remaining three patients had ulcerative lesions of the gut (Table II).

Case 19.—A woman aged 38 had regional ileitis. During the active phase of her disease her serum albumin was 2.2 g./100 ml. and the faecal excretion of P.V.P. was 3.6%. During remission the serum albumin rose to 3.4 g./100 ml. and her P.V.P. fell to 0.1%.

Case 20.—A boy of 16 had cirrhosis of the liver of the juvenile "active" type (Bearn *et al.*, 1956). The serum albumin level was 3.5 g./100 ml. and the ^{131}I-P.V.P. excretion less than 0.05%. Some three months later typical ulcerative colitis developed explosively, and a further month later his serum albumin level had fallen to 2.4 g./100 ml. and his ^{131}I-P.V.P. excretion had increased to 3.4%. Three months later still, during a quiescent phase of his colitis, his serum albumin level had risen to 4.2 g./100 ml. and the ^{131}I-P.V.P. excretion had fallen to the normal level of 0.4%.

Case 21.—A man aged 26 had ulcerative colitis, and during the active stage of his disease had a serum albumin level of 2.8 g./100 ml. and a high excretion of ^{131}I P.V.P. in the faeces (3.4%). After steroid treatment his serum albumin level rose to 4.2 g./100 ml. and the ^{131}I-P.V.P. excretion fell to 0.5%.

Discussion

Only 35–45 g. of dietary protein a day is needed to maintain good health and vigor and to produce nitrogen balance. This was dramatically demonstrated many years ago by Dr. Chittenden, who, after a vigorous professional life on 45 g. of protein daily, climbed the Matterhorn in late middle age. In addition, hypoalbuminaemia is a late manifestation of simple starvation (Keys *et al.*, 1946), and so impaired absorption of protein would have to be far greater than that usually observed to explain the hypoproteinaemia associated with gastro-intestinal disease.

P.V.P. is an inert large-molecular substance which presumably follows similar pathways to albumin, but it is not metabolized in the same way. It is not perfect

as an albumin marker, because each batch contains a large variety of molecular sizes, of which only the majority have a molecular weight of about 40,000 (compared with the molecular weight of albumin, which is 69,000). The shape and the charges on the P.V.P. and albumin molecules are also different. P.V.P. injected intravenously is partially phagocytosed by the reticulo-endothelial system and is de-iodinated (Ravin *et al.*, 1952). The free iodine is excreted in the urine, and this explains the much higher recovery of free iodine in the urine of patients in the first 24 hours after intravenous P.V.P. compared with intravenous ^{131}I albumin. This also causes the blood level to fall more rapidly. A small amount of faecal ^{131}I P.V.P. therefore may represent an appreciable loss of albumin into the gut.

There are also other reasons why one should not expect an exact quantitative relationship between serum albumin and faecal ^{131}I-P.V.P. excretion even if loss of protein into the gut is the only cause of the hypoproteinaemia. These are (*a*) the serum albumin level does not necessarily reflect the total body albumin; (*b*) loss of protein from the gut may fluctuate; and (*c*) ^{131}I P.V.P. exuded into the gut is not completely recovered in the faeces. In fact, only a rough correlation was found in these patients and by previous workers (Gordon, 1959b; Jarnum and Schwartz, 1960; Steinfeld *et al.*, 1960). Nevertheless, these considerations do not detract from the test's empirical value when performed under standardized conditions, and the results of serial observations underline the relationship between hypoproteinaemia and ^{131}I-P.V.P. loss into the gastro-intestinal tract.

The patient with giant rugal hypertrophy of the stomach is of interest, for it was in such a patient that gastro-intestinal loss of protein was first demonstrated to be of importance in the aetiology of hypoalbuminaemia (Citrin *et al.*, 1957). The loss may be due to an exaggeration of the normal exudation of albumin into the stomach (Wetterfors *et al.*, 1960) due to the increased gastric surface area or there may be increased permeability of the gastric mucosa to albumin. The response to surgery has been reported by Schwartz and Jarnum (1959).

The increased loss of ^{131}I P.V.P. in idiopathic steatorrhoea has been reported by Schwartz and Jarnum in one patient and has also been observed by Parkins (1960) in four of a series of 10 patients, although he found no correlation with serum albumin levels. Of our four patients only one had a high faecal P.V.P. excretion, and she also was the only one with a low serum albumin. The mechanism is unknown, and certainly the usual biopsy findings give no structural basis for the increased permeability to protein, nor does the structural abnormality recover during a clinical remission while the patient is on a gluten-free diet. This is in contrast to some patients with idiopathic hypoproteinaemia; for Fraser (1960) has observed mucosal lacteal dilatation in the intestinal biopsy of one patient and suggests that lymphatics weep into the gut and cause the loss of protein. Gordon (1959b) has suggested a similar mechanism. On the other hand, some patients who have been diagnosed as having idiopathic hypoproteinaemia subsequently prove to have overt gastro-intestinal disease (Holman *et al.*, 1959). Any patient who has hypoproteinaemia of unknown cause needs a very careful investigation of the gastro-intestinal tract. This should include the ^{131}-P.V.P. test, small-bowel biopsy, and, in some cases, even laparotomy.

Summary

The ^{131}I-polyvinylpyrolidone test has been performed on 21 patients with a variety of gastro-intestinal disorders, of whom 12 had a low serum albumin. Eleven of these 12 had a high faecal excretion of ^{131}I P.V.P.

Serial studies on six patients showed fairly good correlation between the ^{131}I-P.V.P. faecal excretion and the activity of the underlying disease.

Hypoalbuminaemia in three patients with cirrhosis and two with the nephrotic syndrome did not cause a high P.V.P. excretion in the faeces.

These results lend support to the suggestion that increased loss of protein into the gut, rather than impaired synthesis, is the important factor in causing hypoalbuminaemia in most patients with gastro-intestinal disorders.

We thank all the physicians and surgeons of the Royal Free Hospital and elsewhere who allowed us to study their patients; Drs. Frank Iber and Wade Volwiler for allowing us to quote data on their patients; and Dr. Patricia Wilkinson for performing the albumin turnover in Case 1.

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Addressing a conference of the British Student Health Officers' Association, Mr. J. B. Burnett (Edinburgh) said that during a survey of the teeth of students at the University of Edinburgh comparisons were made between 549 Scottish and 510 English students. The figure for teeth decayed, missing, or filled (DMF) in the Scottish group was 17.9—considerably higher than that of 16.5 for the English group. Scotland and England were then divided into various geographical areas. The highest DMF figure, 18.35, was that of students from the Highlands, and was explained, Mr. Burnett thought, by the scarcity of dentists in that area. The lowest figure, 14.85, was that of the Southern and Eastern counties, probably because there are more dentists there than anywhere in the country. "One nearly always," he said, "finds nice clean mouths showing regular dental attention in people from the South of England." The high figure, 18.0, in the Central Lowlands, was no surprise: "I think there must be more pies, pastries, bread and jam and French cakes eaten in this area than anywhere else in the world."

FIBRINOLYTIC TREATMENT OF CORONARY THROMBOSIS

A PILOT STUDY

BY

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The therapeutic use of fibrinolytic preparations in thromboembolic disease was foreseen when the dissolution by human plasmin (fibrinolysin) of artificially induced thrombi in experimental animals was demonstrated by Cliffton and his colleagues in 1954. Subsequently good results were claimed for the therapeutic effect of plasmin in human subjects with a variety of thrombotic manifestations (*Angiology*, 1959). The possibility of treating coronary thrombosis in man by fibrinolytic means was foreshadowed by the experimental work of Ruegsegger *et al.* (1959). Artificial clots were induced in the coronary arteries of dogs, some of which were then infused with thrombolysin (human plasminogen activated by streptokinase). Serial coronary arteriograms showed that in the control animals the clots persisted up to 15 hours with no more than 20% reduction in size; in those infused with thrombolysin, progressive reduction in the size of the clots was evident within two hours, and by three to seven hours complete lysis had occurred in half and a reduction in size of 60% or more in the remainder. This was confirmed by post-mortem dissection, and histological examination of the infarcts showed that in the treated animals there was less oedema in the marginal areas, less fibrinous epicarditis, and less dilatation of capillaries with no microthrombi to be found in them. These findings obtained even with incomplete lysis of the primary thrombus, suggesting that the plasmin had penetrated the infarct by collateral perfusion. The possibility of a real advance in the treatment of acute coronary thrombosis thus presented itself: early administration of plasmin might re-establish the coronary circulation and minimize permanent damage to the myocardium.

Moser (1958) first reported a case of myocardial infarction treated with plasmin. The use of fibrinolytic agents in a larger number of cases has been reported by Cliffton (1959), deLeon *et al.* (1959), Fletcher *et al.* (1959), Richter *et al.* (1960), and Boucek and Murphy (1960), who gave plasmin by intermittent injection through a catheter passed to the base of the aorta. Fletcher *et al.* and Boucek and Murphy claimed that the treatment caused a more rapid rise and fall in the serum transaminase levels as compared with the controls.

The Present Study

The three principal objects were to establish whether the preparation to be used in the treatment of human coronary thrombosis was safe, whether it was potent *in vivo*, and whether it had a beneficial effect on the course of the disease. The material, thrombolysin, is derived from human plasma which is rich in plasminogen, activated by purified streptokinase, the final product consisting of plasmin and an excess of activator.

Observations were made to determine whether thrombolysin produced the same side-effects as have been reported with other streptokinase preparations—namely, fever, vomiting, and hypotension—and also whether it predisposed to excessive haemorrhage or cardiac rupture. The potency of the preparation was assessed by estimating the fibrinolytic activity of the plasma before, during, and after infusion, and by parallel estimation of plasma fibrinogen levels.

Conclusive evidence of a beneficial effect from the treatment must await the results of a prolonged study with a large number of patients. In the meantime, since it was regarded as unjustifiable to perform coronary arteriography before and after treatment, more indirect methods of assessment have been employed. Observations were made of the duration of pain, the pyrexial reaction, the clinical progress and complications, the evolution of the electrocardiogram, the mortality, and, after recovery, the degree of cardiac insufficiency. It was also thought that the transaminase curves might well provide good evidence of whether the infarct had, in fact, been modified by the treatment. Reperfusion by lysis either of the primary thrombus or of thrombi in the collateral channels might result in a more rapid liberation of enzyme in the treated patients, represented by a higher and earlier peak and a more rapid descent.

Selection of Patients

The patients studied had all been admitted to hospital within 12 hours of the onset of pain. The only grounds for exclusion were the occurrence of episodes of prolonged pain during the days or hours preceding the acute onset (suggesting that minor infarction and liberation of transaminase had already taken place) or obviously imminent death. All patients included had electrocardiographic evidence of fresh infarction at the time of admission except one in whom it subsequently developed. The presence of a Q wave as proof of infarction was not insisted upon as it is often not obtainable in early tracings even of fully transmural necrosis. After the first six, who all received thrombolysin, patients were allotted to the treated or control groups alternately in order of admission, except for a short period when, owing to a shortage of supplies of thrombolysin, successive patients were accepted as controls.

The total number of patients included was 33, of whom 17 (15 men and 2 women) received thrombolysin, and 16 (15 men and 1 woman) were controls. The average age of the treated group was 60.2 years (range 36–80) and of the controls 59.4 years (range 47–72). A history of angina pectoris was elicited from eight of the treated patients and from ten of the controls, and three in each group had had previous myocardial infarcts. The average time elapsing from the onset of pain to the beginning of treatment was 6.3 hours in the treated group (range 3.25–12) and 6.3 hours in the control group (range 2.25–10.25).

Technique of Investigation and Treatment

As soon as the patient was judged suitable for the study a sample of venous blood was collected for

baseline estimation of enzyme levels, fibrinogen content, and fibrinolytic activity (without use of a tourniquet). A wide-bore unbevelled " polythene " cannula was then inserted into a forearm vein and advanced, usually to the elbow, where the junction of a tributary permitted easy withdrawal of further samples. This cannula was kept patent by a slow drip of 3.8% sodium citrate solution. Another polythene cannula of fine bore, or a Guest-type metal cannula, was inserted into a vein of the opposite forearm, and through this the infusion was given, using a children's type of giving set with a 100-ml. cylinder. In the treated cases, 25,000 units of thrombolysin freshly dissolved in 60 ml. of 5% glucose in water were infused rapidly over a few minutes and followed by a further 25,000 units slowly over the next hour. Thereafter 50,000 units in 60 ml. were given hourly for the next 11 hours, making a total dosage of 600,000 units. In the control cases glucose solution was used without the addition of thrombolysin. At the end of the 12-hour period this cannula was withdrawn, but the wide-bore cannula was retained in the other arm until the end of the third day, for the purpose both of obtaining samples of blood and of administering heparin; it was kept patent by a slow drip of 4.1% glucose in N/5 saline.

Blood for serum transaminase estimations (S.G.O.-T.) was withdrawn every four hours for three days, then once daily (by venepuncture) for 10 days. Blood for plasma fibrinogen estimation was withdrawn every four hours for 16 hours, then daily for 12 days. Samples for determination of fibrinolytic activity were withdrawn (without use of a tourniquet) at 5, 10, 15, 30, and 60 minutes after the beginning of the infusion, then two-hourly until its completion and half-hourly for a further three hours. The above routine was modified for the later patients of the series when the estimation of fibrinolytic activity was omitted. Only one cannula (wide-bore) was used for both infusion and withdrawal of samples, care being taken not to lose dead-space thrombolysin, and in these cases citrate solution was not necessary.

Routine anticoagulant therapy was begun as soon as the last specimen for fibrinolytic activity had been obtained. Heparin was administered by drip for 36 hours, and phenindione was continued on a long-term basis. Morphine was given liberally in the event of chest pain, and mephentermine or noradrenaline was administered if shock was profound. If considered necessary, oxygen, digitalis, quinidine, diuretics, and antibiotics were also given.

Twelve-lead electrocardiograms were recorded every eight hours for the first two days, then daily for a further 10 days, and a record was kept of temperature, pulse or apex rate, blood-pressure, and fluid intake and output. The patients were normally kept in hospital for three weeks, and arrangements made for regular follow-up attendance.

Methods

Serum transaminase (S.G.O.-T) was estimated by the method of Reitman and Frankel (1957). Sigma Chemical Company reagents were used.

Plasma fibrinolytic activity was estimated by a method based on that of Fearnley *et al.* (1957) modified by Dr. A. S. Todd in order to shorten the lysis time to a more practical range and to permit the estimation to be made at leisure. To 1.7 ml. of phosphate buffer, *p*H 7.4 (Billimoria *et al.*, 1959), in an ice-bath, was added 0.1 ml. of blood and mixed by inversion. To this was added 0.1 ml. of thrombin solution (Parke Davis) diluted in physiological saline at 0° C. to give 20 units per ml., and again mixed by inversion. The mixture was allowed to clot, then was deep-frozen to lyse red cells. The clots were observed in tubes in a water-bath at 37° C., and the time at which they began to disintegrate was taken as the fibrinolysis time. In nine normal subjects the range was 240 to 540 minutes with a mean of 340 minutes.

Plasma fibrinogen was estimated by precipitating the fibrinogen by the method of Harrison (1947) and measuring the protein content colorimetrically by the method of Hiller *et al.* (1927).

Results

Potency of the Preparation.—The fibrinolytic activity in 10 treated cases and six controls is shown in Figs. 1 and 2. Along the ordinates are plotted logarithmically the reciprocals of the lysis times in minutes multiplied by 10,000, so that figures above the 10,000 mark

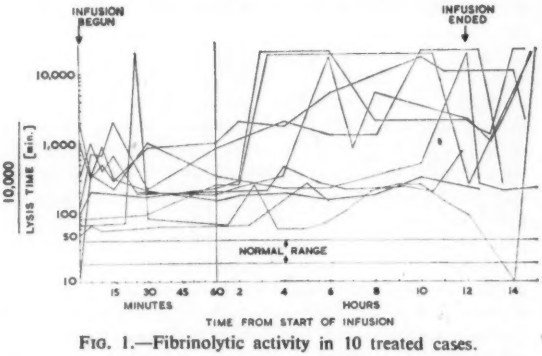

FIG. 1.—Fibrinolytic activity in 10 treated cases.

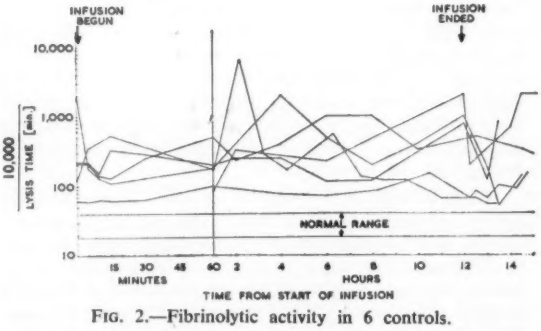

FIG. 2.—Fibrinolytic activity in 6 controls.

represent lysis times of less than one minute, indicating intense fibrinolytic activity. Along the abscissae are plotted the times from the beginning of the infusion. It will be seen that although the levels fluctuated greatly and in all patients they were above the normal range, only one of the control patients, and on a single occasion, exceeded 2,000 units of activity. Among the treated group, however, the levels of five patients reached or exceeded 2,000 units during a substantial part of the infusion, and only one of these was receiving a pressor drug at the time. Figs. 3 and 4 show the results of plasma fibrinogen estimations. There is no striking difference between the two groups, but in five

of the treated patients levels fell below 0.2% and in two instances to zero. Correlation between these levels and the fibrinolytic activity was not close, but in one patient the fibrinogen was absent when the lysis time was under one minute.

Side-effects. — (1) *Fever*: The pyrexial reaction recorded did not differ between the two groups either in the time of onset or in the height or duration of the fever. Only one patient, a control, experienced

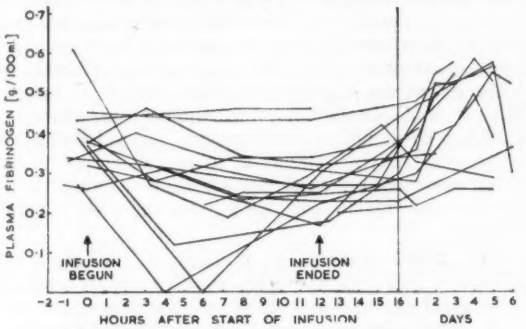

FIG. 3.—Plasma fibrinogen in 16 treated cases.

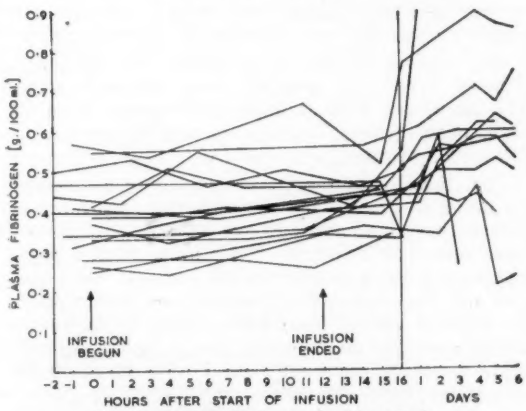

FIG. 4.—Plasma fibrinogen in 16 controls.

a rigor, and it was not followed by fever. (2) *Hypotension*: Although the average fall in systolic pressure in the treated group (25 mm. Hg ± 7) and the controls (23 mm. Hg ± 5) did not differ significantly, in three treated patients the fall was such as to require pressor drugs, and it cannot be stated with certainty that this was not the effect of thrombolysin. No other side-effects were encountered.

Clinical Effects.—In general, thrombolysin infusion, although well tolerated, produced no striking change. Accurate records of the severity and duration of pain were vitiated by the liberal use of morphine, but there was no obvious benefit from the treatment.

Mortality.—Details of the deaths are shown in Table I. It will be seen that five treated patients died and only one control. No important conclusions can be drawn from the necropsy findings, though it may be of interest that the thrombus in the control patient extended distally into the infarct, whereas in the two treated patients who had a fresh thrombus the vessel beyond it was in each case patent.

Post-infarction Angina and Myocardial Insufficiency.—The number of patients in each group who suffered from these conditions before the current infarct or developed them afterwards was too small for comparison to be valid.

Electrocardiograms.—The evolution of cardiographic changes has been studied in each patient from the tracings taken on admission, at 24 hours after the onset of pain (that is, shortly after completion of the infusion), at 7 days, at 21 days, and at the three-month follow-up visit. From the unipolar limb leads and from the chest leads V2 to V6 a measurement was made of the greatest pathological Q wave, and the number of leads in which such a wave appeared. A similar estimate was made of the ST elevation and T-wave inversion. The mean figures for each group are presented in Table II. There was very little difference between treated and controls except that the T-wave inversion at 24 hours was much less in the treated group. By seven days this difference had disappeared.

Transaminase Curves.—The transaminase levels for each patient were plotted against the time of the onset of pain, and the curves produced varied greatly from one patient to another according to the severity of the infarct. The characteristic form consisted of a steep

TABLE I.—*Deaths*

Age and Sex	Series	Hours after Onset to Infusion	Time after Onset to Death	Mode of Death	Necropsy Findings
78 F	Treated	5½	14 hours	Hypotension	Infarct with partial rupture. No thrombus
69 F	,,	7½	6 weeks	Congestive failure	Many old thrombi. 6-week infarct and haemorrhage into atheromatous plaque
50 M	,,	12	1 year	,,	No necropsy
49 M	,,	8½	8 weeks	,,	Old thrombi in R. and L. cor. art. 8-week thrombus in interventricular branch with infarct
80 M	,,	4	27 hours	Hypotension	Fresh thrombus and infarct
60 M	Control	5½	2 weeks	Broncho-pneumonia and hypotension	,, ,,

TABLE II.—*Electrocardiograms (Mean Figures)*

Series		Initial	24 Hours	7 Days	21 Days	3 Months or More
		Q Waves				
Treated	Greatest depth (mm.) ..	4	6	7	5	4·1]
	No. of leads involved ..	1·5	2	2	2	1·6]
Control	Greatest depth (mm.) ..	3	5·5	7	5	5·6
	No. of leads involved ..	2	2	2	2	1·9
		ST Elevation				
Treated	Greatest height (mm.) ..	4	2	1·3	1	0·5
	No. of leads involved ..	3	3	2·4	2	1
Control	Greatest height (mm.) ..	2	1·5	1·5	1	0·6
	No. of leads involved ..	2·5	3	2·5	1·7	1·2
		T-Wave Inversion				
Treated	Greatest depth (mm.) ..	0·9	1·8	1·6	5·2	1·1
	No. of leads involved ..	0·8	2·3	2·4	3·3	2
Control	Greatest depth (mm.) ..	1	3·8	1·7	5·8	1·6
	No. of leads involved ..	1·4	3·2	2·5	3·8	3

and linear ascent, a sharp peak, a rapid descent to about 50% of the total fall, and thereafter a more gradual decline until the resting level was reached about the seventh day. Unfortunately in several of the patients, for various technical reasons such as haemolysis of the samples, the curves obtained were incomplete and when the deficiencies involved the peak of the curve these results could not be included in the analysis. Fully reliable curves were available from 10 treated patients, and these have been matched against the first 10 satisfactory curves from controls. They have been analysed individually in respect of a number of parameters, and the mean figures for the two groups are compared in Table III. Contrary to what has been previously reported (Fletcher *et al.*, 1959; Boucek and Murphy, 1960) the peak was not attained sooner in the treated

TABLE III

	Average Control	Average Plasmin	t_{18}df.	P
Hours from onset to peak ..	23·9	26·5	0·81	40%
Days from peak to resting level	7·7	6·6	0·94	35%
Rate of rise (units/hour) ..	11·6	16·2	0·99	30%
Peak* (S.F. units)	221	283	0·77	45%
Rate of fall from peak to halfway (units/hour) ..	9·1	28·2	1·35	20%
Area (unit-days)	410	381	0·32	75%
Rate of rise peak	0·050	0·046	0·36	70%
,, ,, rise/area	0·031	0·044	1·07	30%
Peak/area	0·634	0·918	2·36	3%
Rate of fall/peak	0·326	0·054	1·74	10%
,, ,, fall/area	0·021	0·057	1·78	10%

* Analysis based on logarithms.
In order to be significant at 5% level, t_{18} must exceed 2·1, and at 1% level t_{18} must exceed 2·9.

cases. The rate of rise and, still more, the rate of fall were greater in the treated group but not to a significant degree. The height of the peak and the area underlying the curve likewise did not differ significantly in the two groups. When, however, the ratio of peak to area was calculated for each patient, the mean of the results was significantly greater in the treatment group. Also, when the rate of fall was similarly related to peak and area the differences between the two groups began to approach significance, though they did not attain it. It would seem, therefore, that, *provided the two populations are comparable in respect of the extent of original myocardial injury*, thrombolysin has had the effect of making the transaminase curves taller and narrower, and this is in keeping with our original concept of what might be expected.

Discussion

The object of using this treatment for coronary thrombosis was to dissolve the thrombus so that the infarct which must inevitably ensue if the artery has been occluded for more than 60 minutes (Savranoglu *et al.*, 1959) would be reperfused and consequently modified in its evolution. It must be realized, however, that the experimental conditions upon which the clinical trial was based differed in important respects from those obtaining in human disease. In the experiments on dogs a fibrin clot was produced in a segment of healthy artery, whereas in the human subject fibrin and platelet thrombi have in most instances been deposited on the surface of atheromatous plaques, which have already narrowed the vessel to a greater or less degree. Such thrombi might well be more resistant, and if lysed might leave a permanent constriction that would impede the flow of blood and even cause it to cease if hypotension should supervene. In this respect collateral perfusion of the margins of the infarct is an important possibility.

The dose of thrombolysin to be given was arbitrarily selected so as to strike a balance between the safe and the effective. Although it might have been theoretically desirable to assess the requirement of activator for each patient in relation to the level of streptokinase antibody, the time consumed would have rendered most difficult the early institution of treatment which was essential to the trial. In the event, the average time from onset of pain to commencement of infusion, 6.3 hours for both groups, is probably as short as can reasonably be expected in hospital practice. Similarly it was thought that an interrupted course of treatment on successive days, as adopted by Richter *et al.* (1960), would only make the effects of treatment more difficult to assess. Heparin and phenindione were withheld for the first 15 hours so as not to interfere with the estimation of fibrinolytic activity. Reports of the effects of these drugs upon such activity have been conflicting (Von Kaulla and McDonald, 1958; Moser and Hajjar, 1960).

Our results confirm the findings of Lackner and Merskey (1960) that most patients with acute myocardial infarction have a greatly enhanced fibrinolytic activity in the blood. In several of our treated group, however, the activity was much greater than in the controls, having risen from comparable initial levels, and it is concluded that this was the effect of the thrombolysin.

The absence of serious side-effects was gratifying, although hypotension may have been induced in a few. The temporary disappearance of fibrinogen from the blood of two patients caused some disquiet, but was not followed by further complications.

The clinical results of treatment have demonstrated no dramatic change, and although five of the treated patients have died and only one control, firm conclusions cannot be drawn from this in so small a series, and must await a more extended trial. It was hoped that the electrocardiograms might have demonstrated the effect of therapy upon the evolution of the infarct, and it is perhaps disappointing that in the development of Q waves, ST elevation, and T-wave inversion the two groups have not differed significantly.

The transaminase curves, therefore, remain in this study the sole evidence of a significant difference between the treated and the untreated. If, by extending the trial, it can be shown with certainty that the two groups are identical in respect of the extent of the original injury, then they may provide evidence of the treatment having a significant effect upon the infarct. Only many more necropsies, however, will show definitely whether this effect is obtained by removing the thrombus from the obstructed vessel, by recanalizing collaterals, or by some other process. Only further study, too, will show how important are fibrinolytic mechanisms in the natural evolution of cardiac infarction in man, and to what extent it may be possible to use artificial fibrinolytic agents as a means of treatment.

Summary

A series of 33 patients suffering from coronary thrombosis of less than 12 hours' duration have been included in a preliminary clinical trial in which 17 of them were treated with a fibrinolytic preparation and 16 served as controls.

A greater degree of fibrinolytic activity in the blood has been demonstrated in a sample of the treated

patients than in a sample of the controls. In a few of them there was also a significant fall in the level of fibrinogen.

The fibrinolytic agent did not produce any febrile reactions, but it may occasionally have caused hypotension.

The numbers included in this pilot study were too small for differences in mortality to be significant. There were no definite differences in the clinical response of the two groups, nor in the evolution of the electrocardiographic changes.

Detailed transaminase curves have been prepared and appear to differ significantly in one respect—namely, the peak area ratio, which is greater in the treated group. The implication of this is discussed.

A more extended trial is in progress.

Our thanks are due to colleagues at the Royal Victoria Infirmary and many practitioners who referred cases to us; to the following house-physicians—Drs. Ansah, Burdus, Campbell, Kinlen, Sanderson, Todd, Varde, and Waring, who gave a great deal of medical care; to the matron, Miss F. Shaw, and her staff for devoted nursing care; to Dr. A. L. Latner and his staff for biochemical facilities; to Drs. A. Todd and P. Stephenson for help with fibrinolysis; to Professor J. B. Duguid and Dr. P. A. Ellis for necropsy examinations; and to Mr. D. J. Newell for statistical assistance. Finally, we are indebted to Messrs. Merck Sharp and Dohme for generous supplies of thrombolysin.

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Reporting that more teachers are flying from England to New Zealand, *The Times* (August 31) records the following comment by one of them: "The pay here is not high enough to compensate for this land's stinking, dying attitude. My wife and I are escaping from the typical overcrowded and lethargic existence of this welfare state. We and many other teachers here are sick to death of this country. Lack of pay is certainly an important factor, but it is only one of the criticisms we can justifiably level against England to-day."

LIVER FUNCTION IN ACUTE MYOCARDIAL INFARCTION

A STUDY USING BROMSULPHTHALEIN TEST

BY

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The bromsulphthalein (B.S.P.) test is regarded as one of the most sensitive biochemical tests of liver function (Rosenthal and White, 1925; Sherlock, 1955). It is well known that disturbances of liver function occur commonly in cardiac disease. They range from transient abnormalities of liver function, such as occur in reversible congestive cardiac failure (Evans *et al.*, 1952b), to a true cardiac cirrhosis. In states of acute cardiac damage, such as myocardial infarction, jaundice may appear, and excess urobilinogen has been noted in the urine for several days after an attack (Evans *et al.*, 1952a; Koskelo, 1956).

It was therefore decided to investigate liver function by the B.S.P. test in an unselected group of cases of acute myocardial infarction. These results were compared with those of other methods of detecting liver dysfunction.

Material and Methods

A group of 20 patients (15 men and 5 women) aged from 40 to 72 years was studied. Each was admitted with acute myocardial infarction and was examined by me within a few hours of admission. Clinical shock was diagnosed by the following criteria: cold, pale skin, sweating, cyanosis, thready pulse, and hypotension. Blood was taken for the estimation of haemoglobin, serum bilirubin, thymol turbidity, zinc sulphate turbidity, alkaline phosphatase, and blood urea. The B.S.P. test was performed by injecting 5 mg. of B.S.P. per kg. body weight, and specimens were taken after 5 and 45 minutes. The results reported are the percentage retention of B.S.P. in the blood after 45 minutes, the normal being less than 6%. The sample was compared with a standard solution of B.S.P. at a concentration of 10 mg./100 ml., which is theoretically the level of B.S.P. equilibrated throughout the serum in the dose administered.

Results

Clinical details and results of the B.S.P. tests are shown in the Table. Fifteen patients (75%) had abnormal B.S.P. retention within a few hours of myocardial infarction. Of these, three died within three weeks. In eight patients the B.S.P. test was repeated 7–10 days after admission, and was still abnormal in four cases. One year later, B.S.P. retention in three of these patients was 3%, 10%, and 12%. In five patients (25%) it was normal at the time of admission. Shock was diagnosed in two of these patients, one of whom died a few months later. Abnormal B.S.P. retention was more marked in patients who were shocked ($26\% \pm 18.2\%$) than in those who were not ($14.9\% \pm 13.3\%$), but the differences do not reach statistical significance because of the large variance. There was no correlation between abnormality of the B.S.P. test and elevation of the blood urea, the latter being a reflection of reduced renal blood flow.

Discussion

The study reported here was carried out on patients with no previous hepatic dysfunction, and in whom other tests of liver function were in general normal. In the 24 hours after acute myocardial infarction 75% had abnormal B.S.P. retention. These findings contrast with those of Evans *et al.* 1952a), who found normal B.S.P. retention in all those cases of their series in which this test was performed. They do not state, however, how long after the infarct they carried out the test.

There are two possible explanations for abnormal B.S.P. retention in the circulation. Either impairment of intrinsic hepatic-cell function may reduce the uptake of B.S.P. by the liver from the plasma, or reduction or diversion of hepatic blood flow diminishes the amount of B.S.P. presented to liver cells, and results in increased retention in the plasma.

Centrilobular necrosis in cases of fatal myocardial infarction was described by Clarke (1950). This change occurs particularly when shock and hypotension have been present for more than 24 hours (Ellenberg and Osserman, 1951). The present study shows that the results of B.S.P. tests tended to be abnormal more often in patients who were shocked, and that when this was severe initially B.S.P. retention remained abnormally high after 7–10 days. As there was no clinical evidence of systemic venous congestion in any case on admission to hospital, hepatic changes could not be attributed to this cause.

On the other hand, the mechanism of uptake of B.S.P. by the liver may partly account for these results. Normally, when B.S.P. is injected intravenously it is rapidly bound to plasma protein, and is cleared from the circulation, mainly by the liver, if there is normal biliary secretion (Ingelfinger *et al.*, 1948). An important factor in this selective capacity of clearance of B.S.P. from the plasma is the anatomical circulatory arrangement of the liver (Brauer and Pessotti, 1949). Depression of this circulation may therefore reduce the amount of B.S.P. which comes in contact with the hepatic cells in a given time, and also impair the functional capacity of the cells to remove it from the plasma. Hence the rate of disappearance of B.S.P. from the plasma would be diminished. In shock, not only is the blood flow to the liver reduced, but there is also experimental evidence of an arterial shunt which by-passes the liver (W. H. H. Andrews, 1959, personal communication). Increased retention of B.S.P. in the circulation in cases of myocardial infarction may thus be partly due to alteration in the blood supply to the liver. When systemic shock is present, hepatic blood flow in these cases would tend to be reduced. This may account for the finding that 9 out of 11 patients in this series who were clinically shocked on admission had abnormal B.S.P. retention.

It is well known that in shock renal blood flow is reduced, with a consequent rise in the blood-urea concentration. The results in the Table do not show any consistent relationship between increased B.S.P. retention and rise of blood urea. This may be explained by the different degrees of alteration of blood flow to the liver and the kidney in these cases, possibly due to the differing modes of oxygen utilization by these organs.

Summary

In a series of 20 patients with acute myocardial infarction studied within the first 24 hours of the onset of pain, abnormal B.S.P. retention was found in 15. This was more marked in the presence of shock. There was no significant correlation between abnormal B.S.P. retention and elevated blood urea. Other liver-function tests were normal.

The mechanism of B.S.P. uptake by the liver is discussed, and it is suggested that reduction in blood

Clinical Features and Liver-function Tests

Case	Sex and Age	History and Clinical Features	B.P. on Admission	Blood Urea mg./100 ml.	Liver-function Tests	B.S.P. at 45 Minutes	
						On Admission	7 to 10 Days Later
1	F 71	12 hours' pain. Shocked. Died 3 weeks later from progressive heart failure	140/100	81	Normal	64%	40%
2	F 61	6 hours' pain. Shocked. Increased jugular venous pressure	105/70 Later 75/50	46	,,	41%	22%
3	F 50	4 hours' pain. Mild shock and cyanosis	115/80	26	,,	35%	3%
4	F 54	Hypertensive diabetic. 6 hours' pain. No shock	200/130	41	,,	8%	—
5	F 51	6 hours' pain. Pericardial rub. No shock	115/70	31	,,	26%	5%
6	M 62	6 hours' pain. Shocked. Increased jugular venous pressure	90/65	64	Serum bilirubin 1–3 mg./100 ml.	17%	12%
7	M 63	Less than 4 hours' pain. Not severely shocked, but increased jugular venous pressure	110/85	44	Serum bilirubin 1 mg./100 ml.	34%	7%
8	M 58	9 hours' pain. Severe. Died 10 days later from peripheral circulatory failure	110/85	39	Normal	34%	—
9	M 51	12 hours' pain. Severe shock. Died 7 days later from peripheral circulatory failure	85/75	91	,,	13%	—
10	M 54	2 hours' pain. Not shocked	110/85	40	,,	34%	5%
11	M 47	3 hours' pain. Not shocked	100/65	—	,,	9%	—
12	M 66	6 hours' pain. Not shocked	115/70	35	,,	7%	—
13	M 49	Intermittent pain for 1 week	105/70	32	*Alkaline phosphatase 26·3 units	43%	—
14	M 57	12 hours' pain. Shocked. Large doses of morphine given. Required hydrocortisone and mephentermine	90/70	41	Normal	17%	6%
15	M 59	6 hours' pain. Not shocked, but moderate rise in jugular venous pressure	110/80	61	,,	12%	3%
16	M 72	6 hours' pain. Mild shock. Given I.V. hydrocortisone. Died a few months later	100/60	46	,,	0%	—
17	M 55	3 hours' pain. Moderate rise of jugular venous pressure and minimal shock	95/70	28	,,	5%	5%
18	M 45	4 hours' pain on previous day. Not shocked	160/80	52	,,	4%	—
19	M 45	3 hours intermittent pain. Not shocked	170/90	26	,,	4%	—
20	M 40	1 hour's pain and residual ache. Minimal cyanosis. Not shocked	135/95	20	,,	3%	—

Cases 1–15 showed abnormal B.S.P. on admission to hospital; Cases 16–20 showed normal B.S.P. tests. In cases marked with —, B.S.P. tests were not repeated 7–10 days after admission. *Clinically well 1 year later. Alkaline phosphatase 8·6 units ; B.S.P. 11%.

flow to the liver is an important factor causing alteration in the B.S.P. test in cases of acute myocardial infarction.

The patients were under the care of Dr. J. Gibson Graham and Dr. H. Conway, whose co-operation I gratefully acknowledge. I thank Dr. A. Goldberg, University Department of Medicine, Western Infirmary, Glasgow, for help in preparing this paper; and Mr. W. Plenderlith for his technical assistance in carrying out the B.S.P. tests.

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A SYNDROME DUE TO THE BACTERIAL COLONIZATION OF SPITZ-HOLTER VALVES

A REVIEW OF FIVE CASES

BY

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The treatment of hydrocephalus has been advanced by the introduction of non-return valves that shunt the cerebrospinal fluid (C.S.F.) from the lateral ventricle of the brain to the superior vena cava. At this hospital the Spitz–Holter valve has been used, details of which are shown in Fig. 1. The complications of thrombosis and sepsis are each recognized to occur in approximately 10% of cases. Over 120 cases have been treated at this hospital (Cohen, 1961, unpublished), and in the group complicated by sepsis we have differentiated a new syndrome—persistent bacteraemia—which is characterized by persistent pyrexia, progressive anaemia, splenomegaly, and positive blood cultures. Previously these cases have been included with the septicaemias, and the attempted eradication of the infection by the use of systemic and intraventricular methicillin has been reported (Callaghan *et al.*, 1961). Five case histories of this syndrome and one of septicaemia are recorded.

Case 1

A male infant born on January 1, 1959, had an occipital encephalocele excised on February 24 and subsequently developed progressive hydrocephalus. A Spitz–Holter valve was inserted on April 4, but needed two revision operations before effective shunting was obtained. (The last operation was on August 2.)

In October the infant began to run a continuous temperature—range 99–102° F. (37.2–38.9° C)—and on investigation was found to have a urinary infection due to *Proteus vulgaris*. This partially responded to sulphadiazine and chloramphenicol (125 mg. q.d.s.), but during the next three months the infant became anaemic (Hb 47%) and needed two blood transfusions to correct this anaemia. As the symptoms persisted further investigations were carried out and *Pr. vulgaris* was then cultured from the blood. At this stage there was no evidence of infection around the valve. On December 12 the infant was put on kanamycin (100 mg. b.d.), which temporarily reduced the pyrexia, but still *Pr. vulgaris* was repeatedly cultured from the blood (Fig. 2). The C.S.F. obtained by direct ventricular puncture was sterile on two occasions. On January 7, 1960, the catheter was removed from the internal jugular vein and the C.S.F. allowed to drain externally into a container. This C.S.F. was found to be clear and colourless, contained 3 leucocytes per c.mm., yet culture produced a profuse growth of *Pr. vulgaris*. After diverting this infected C.S.F. from the blood-stream the temperature returned to normal and urine and blood cultures remained sterile from then on (Fig. 2). Thus it appeared that bacteraemia had been controlled.

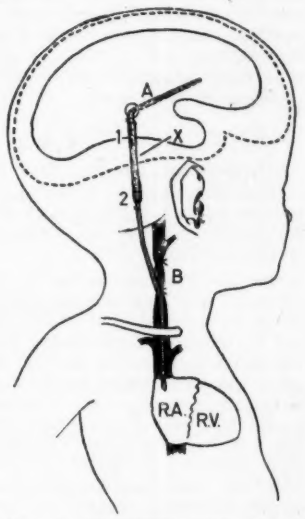

FIG. 1.—Component parts of the Spitz–Holter valve: a proximal ventricular catheter (A); the valve (X) that shunts the C.S.F. from the lateral ventricle of the brain to the superior vena cava or right atrium via the internal jugular catheter (B). These parts are held together and in position by the black silk sutures (1 and 2).

On February 2 (almost one year after its insertion) the valve was removed and *Pr. vulgaris* isolated from all the component parts, indicating colonization of the valve by this organism. As the hydrocephalus was still progressive, ventricular drainage was instituted and C.S.F. draining externally by this method was sterile, confirming that it was the removed colonized valve that had been the source of the bacteraemia. A second valve was inserted on March 31, and this functioned satisfactorily. The child was discharged, but on June 13 he died because of an episode of raised intracranial pressure (16 months after the original operation).

At necropsy there was no evidence of infection, thrombosis, or embolism, but an enlarged spleen was found. This weighed 100 g. and showed marked lymphoid hyperplasia.

Case 2

A male infant born on March 8, 1960, had haemorrhagic disease of the newborn complicated by intraventricular haemorrhage. This led to progressive hydrocephalus and ventriculography demonstrated a basal cistern block. A Spitz–Holter valve was inserted on May 19.

Post-operatively his temperature slowly rose to 101° F. (38.3° C.) and then fluctuated between 97 and 99.5° F. (36.1 and 37.5° C.). On the tenth post-operative day the spleen became palpable and during the next three months enlarged to 2 in. (5 cm.) below the costal margin. Anaemia then slowly developed (Hb 55%) over the next six months, necessitating one blood transfusion. Coagulase-negative staphylococci were cultured from the blood on 15 occasions during the nine months that the bacteraemia was in existence. During this same period coagulase-positive staphylococci were isolated on three occasions, but this was not the organism primarily isolated (see Table).

In spite of intensive and prolonged attempts to eradicate the infection (including penicillin and sulphadiazine, tetracycline, and systemic methicillin for 150 days) the bacteraemia persisted. On March 10 the catheter was removed from the internal jugular vein and C.S.F. allowed to drain externally. This C.S.F. was clear and colourless, contained 9 leucocytes per c.mm., and culture produced a heavy growth of coagulase-negative staphylococci. At the same time C.S.F. obtained by direct ventricular puncture was clear and colourless, contained no cells, and was sterile. The spleen became smaller and after 10 days was no longer palpable, the blood cultures were sterile, and the temperature had returned to normal. The Spitz–Holter valve was removed on April 13, 1961 (11 months after its insertion), and coagulase-negative staphylococci were cultured from all the component parts.

Case 3

A male infant born on June 12, 1959, was noticed to have craniosynostosis. This was later complicated by progressive internal hydrocephalus which was confirmed by ventriculography. A Spitz–Holter valve was inserted on March 10, 1960.

The post-operative period was covered by antibiotics (penicillin and sulphadiazine for 10 days and tetracycline for 10 days), but the temperature rose to 102° F. (38.9° C.) and remained elevated—range 99–102° F. (37.2–38.9° C.). The infant then became anaemic (Hb 44%) and during the next six months needed seven blood transfusions to correct this progressive anaemia. The spleen then enlarged, and by the 12th post-operative week had reached 2 in. (5 cm.) below the costal margin. Coagulase-negative staphylococci were cultured from the blood on 28 occasions during the year that the bacteraemia was in existence, whereas coagulase-positive staphylococci were cultured only three times during the same period (see Table). The patient was given a 50-day course of methicillin by intramuscular and intraventricular injection with marked clinical improvement. The temperature returned to normal, the spleen became impalpable, and finally the blood cultures were sterile. When antibiotic treatment was discontinued he relapsed—the pyrexia recurred, he became anaemic again, and his spleen rapidly enlarged to 4 in. (10 cm.) below the costal margin. A bone-marrow puncture on October 12 showed a "cellular hyperplastic marrow with a shift to the left in the myeloid series."

On October 27 the spleen was removed as it was thought to be the site of abscess formation and by virtue of its size to be causing features ascribed to "hypersplenism." The spleen weighed 150 g. No abscesses were present, but a culture of the spleen grew coagulase-negative staphylococci. Histological examination revealed "considerable quantities of haemosiderin in the pulp and germ centres of the follicles, evidence of an actively progressive haemolytic process." The splenectomy had had the desired effect of reducing the haemolysis, as he needed only one blood transfusion in the five months following this operation. As blood cultures still grew coagulase-negative staphylococci and the temperature remained elevated, the internal jugular catheter was exteriorized on March 14, 1961, and the C.S.F. allowed to drain externally. This was clear and colourless, contained 3 leucocytes per c.mm., yet culture grew coagulase-negative staphylococci, whereas C.S.F. obtained by direct ventricular puncture was sterile. The temperature then returned to normal and the blood cultures were sterile on two successive occasions.

The valve was removed on April 11 (13 months after its insertion); at operation there were no signs of infection around the valve, but on culture of all the component parts coagulase-negative staphylococci were grown, once again indicating colonization. As the hydrocephalus was still progressive a second valve was inserted on April 22, and the patient then progressed favourably and was discharged.

Case 4

A male infant born on December 12, 1959, developed progressive hydrocephalus after a meningitis due to *Escherichia coli*. Ventriculography demonstrated a basal cistern block. A Spitz–Holter valve was inserted on March 31, 1960, and post-operatively he developed a stitch abscess which cleared completely on local treatment.

Six weeks post-operatively the temperature began to rise—range 97–101° F. (36.1–38.3° C.)—and another abscess developed in the region of the upper end of the valve. This, too, healed on local treatment. The temperature, however, remained elevated and his spleen began to enlarge and was palpable 2 in. (5 cm.) below the costal margin. Coagulase-positive staphylococci were isolated from the blood on 10 occasions during the six months that the bacteraemia was in existence, and during the same period coagulase-negative staphylococci were isolated three times.

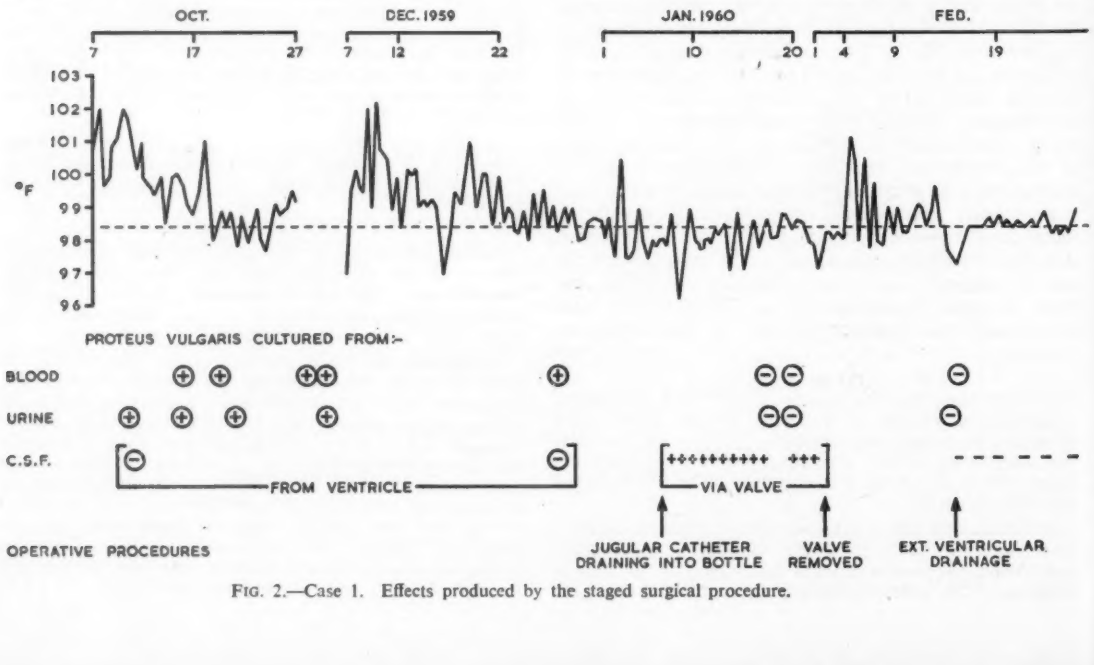

FIG. 2.—Case 1. Effects produced by the staged surgical procedure.

The patient then became anaemic (Hb 48%) and needed five blood transfusions during the next six months. Penicillin and sulphadiazine were then given, followed by chloramphenicol and oleandomycin. The temperature still remained elevated, so he too was put on a course of methicillin by intramuscular and intraventricular injection and then locally, but the bacteraemia persisted despite continuing methicillin for 110 days. On October 27 the valve was removed and coagulase-positive staphylococci were isolated from all the component parts. Since removal of the valve the fever has subsided, the spleen has been impalpable, and coagulase-positive staphylococci have not been cultured from the blood again.

Case 5

A female infant born on March 16, 1958, was noted to have progressive hydrocephalus at a few weeks of age. Ventriculography demonstrated a basal cistern block, and a Spitz–Holter valve was inserted on October 21.

Post-operatively the patient ran a temperature—range 98–101° F. (36.7–38.3° C.)—even though this period was covered by a course of penicillin and streptomycin. No cause for the temperature could be found, and blood cultures were sterile even though she was suspected of having a "bacteraemia." After a period of observation the temperature settled and she was discharged. Attendance at the follow-up clinics was very erratic, and 18 months later the patient was readmitted with a history of malaise, prolonged bouts of fever and several "blue attacks."

On examination the child was marasmic and pale, and her spleen was palpable 4 in. (10 cm.) below the costal margin. The temperature rose to 100° F. (37.8° C.) and the haemoglobin was 29%. Coagulase-negative staphylococci were isolated from the blood on 10 occasions after the bacteraemia had been proved, and during the same period coagulase-positive staphylococci were isolated twice. Once again attempts to control the bacteraemia by antibiotics failed (penicillin by intramuscular and intraventricular injection for 30 days, and methicillin by intramuscular and intraventricular injection for 50 days). The valve was removed on October 27, 1960, (two years after its insertion), and no signs of infection were seen at operation, although coagulase-negative staphylococci were cultured from all the component parts, once again indicating colonization by these organisms. After removal of the valve the child made a rapid recovery—the temperature and haemoglobin level remained normal, and blood cultures were repeatedly sterile. Fortunately, as in Case 4, the hydrocephalus had arrested.

Case of Septicaemia

In contrast with these five cases, the history of an infant who died of a fulminating septicaemia is recorded.

Case 6.—A premature male infant born on April 17, 1960, developed progressive hydrocephalus and had a Spitz–Holter valve inserted on July 28. The post-operative period was covered by a course of penicillin and sulphadiazine. The patient ran a temperature for three days, but this soon settled and he was discharged on the tenth day. Three days later he was readmitted in a critical condition. His temperature was 103° F. (39.4° C.) and a fluctuant swelling was found around the valve. He had signs of consolidation in the right upper lobe of the lung. Despite treatment he rapidly deteriorated and died the following day. At necropsy a large abscess was found around the valve, which appeared to be still functioning satisfactorily. There was adherent thrombus formation in the superior vena cava, and the lungs showed numerous areas of consolidation with early abscess formation and empyema. Coagulase-positive staphylococci were isolated from the lungs, pleura, spleen, and also from the blood taken just prior to his death.

Leucocytosis has not been a prominent feature in these cases, as more than 60% of the white-cell counts performed were normal, and of those that were raised only one exceeded 20,000 white cells per c.mm. The platelets have appeared normal in all cases.

Clinical Manifestations

Case No.	Duration of Disease (Days)	Severity of Anaemia Indicated by: Lowest Hb %	Severity of Anaemia Indicated by: No. of Blood Transfusions Over Six Months	Spleen Size Below Costal Margin: in.	Spleen Size Below Costal Margin: cm.	Organisms Isolated (Frequency in parentheses)
1	120	47	4	0*		*Pr. vulgaris*
2	290	55	1	2	5	Coag.-neg. staph. (15) Coag.-pos. staph. (3)
3	360	44	7	4	10	Coag.-neg. staph. (28) Coag.-pos. staph. (3)
4	200	48	5	2	5	Coag.-pos. staph. (10) Coag.-neg. staph. (3)
5	730	29	6	4	10	Coag.-neg. staph. (10)
6	10	60	0	0		Coag.-pos. staph. (2) Coag.-pos. staph.

*In this patient the spleen was not noted to be enlarged during life but was so at necropsy.

Discussion

Sepsis in the scalp wound or contamination of the operation site may involve the component parts of the valve, and organisms will then be carried into the blood-stream by the flow of the C.S.F. The resulting condition depends to a large extent on the nature of the infecting organisms. If the organisms are of a relatively high degree of virulence (coagulase-positive staphylococci as in Case 6) then inflammation occurs around the valve and a septicaemia with embolic abscesses may ensue. If, however, the organisms are by comparison less virulent (*Pr. vulgaris* as in Case 1, coagulase-negative staphylococci as in Cases 2, 3, and 5) or are rendered so by antibiotics (coagulase-positive staphylococci as in Case 4), then obvious inflammation around the valve does not occur, but the organisms persist in the component parts, resulting in colonization. When this occurs in a functioning valve then sterile C.S.F. from the lateral ventricle is infected in its passage through the valve and is carried into the blood-stream, thereby causing the bacteraemia, which, when compared with the septicaemias, is mild and chronic. All these facts are borne out by the sequence of events in Case 1, which was the first where proof of the natural history of the syndrome was obtained.

This patient had all the signs of a persistent proteus bacteraemia. The valve was not clinically suspect as there was no inflammation around it and the C.S.F. obtained by direct ventricular puncture was sterile. The bacteraemia, however, was terminated by the exteriorization of the internal jugular catheter. In addition, the sterile C.S.F. from the lateral ventricle was persistently infected after passing through the valve (Fig. 2), thereby incriminating the valve. Final proof was obtained when the valve was removed, for, though there was no evidence of inflammation around the valve, the same organisms were cultured from all its component parts. Cases 2 and 3 behaved in a similar manner after the exteriorization procedure described, whereas in Cases 4 and 5 the bacteraemia was terminated by a one-stage removal of the valves. Therefore there exists the condition of colonization of the valve by these comparatively less virulent organisms, and if the valve is functioning it will give rise to a persistent bacteraemia.

The triad of persistent pyrexia, progressive anaemia, and splenomegaly can be explained by the continual contamination of the blood-stream by these organisms of relatively low virulence. This is in strong contrast with the history of the rapidly fatal septicaemia (Case 6) where the virulent coagulase-positive staphylococci produced an abscess around the valve and invaded the blood-stream, causing embolic abscesses in the lungs. Further support for the concept of persistent bacteraemia is that in none of the cases was there any evidence of embolic foci in lung, brain, kidney, bone-marrow, intestinal vessels, or skin.

The treatment of this condition has been described in a separate article (Callaghan *et al.*, 1961). Systemic and intraventricular methicillin did suppress the clinical signs, but relapse was immediate on discontinuing the drug. The only absolute cure was removal of the valve.

In the past few years much attention has been paid to the role of the staphylococcus in human disease. Generally speaking, the coagulase-positive strains have been clearly associated as human pathogens, whereas the coagulase-negative strains were usually regarded as contaminants when obtained in pure culture from the blood. Recently, however, evidence has accumulated to prove that the negative strains cannot always be so regarded (Fleming and Seal, 1955; *Lancet*, 1956, 1958; Smith *et al.*, 1958). The report of coagulase-negative staphylococcal endocarditis after mitral valvotomy has demonstrated the pathogenicity of this organism (Resnekov, 1959), while the natural history of the syndrome described here adds further evidence to this concept. Thus coagulase-negative staphylococci were repeatedly cultured from the blood of patients with the syndrome. After exteriorization of the internal jugular catheter the signs and symptoms all disappeared, the blood cultures became sterile, yet the C.S.F. draining externally still contained the coagulase-negative staphylococci. Finally, culture of the component parts of the valve after removal produced a pure growth of the coagulase-negative staphylococci.

The cases in this series all exhibited mixed infections with coagulase-negative and coagulase-positive staphylococci (see Table). In Cases 2, 3, and 5 the negative strain was the dominant and was cultured first in all three cases, whereas the positive strain was only occasionally cultured. In Case 4 the coagulase-positive strain was the dominant and was repeatedly cultured before the negative strain was isolated. The fact that mixed staphylococcal infections can occur was also noted by Resnekov (1959). He postulated that both organisms were present initially and that the coagulase-negative strains persisted because they were more resistant to antibiotic treatment. In three cases in this series, however, the coagulase-negative staphylococci were the first isolated, so that the full significance of mixed infection remains uncertain.

Summary

A new syndrome—persistent bacteraemia—occurring in cases of hydrocephalus treated by the insertion of a Spitz–Holter valve is described. It is due to colonization of the valve by organisms of relatively low virulence, and is characterized by persistent pyrexia, progressive anaemia, splenomegaly, and repeatedly positive blood cultures.

The coagulase-negative staphylococcus was the causal organism in three of the cases.

We are indebted to Mr. G. H. Macnab for his encouragement, help, and advice, and for permission to use the cases in this series; to the morbid-anatomy and the pathology departments for their help in the multitude of investigations and reports; to the department of medical illustration for the charts; and to the sister and staff of ward 6 C & D of The Hospital for Sick Children, Great Ormond Street, London, for their assistance with the cases.

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PARAESTHESIA OF THE HAND IN PREGNANCY

BY

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Interest in paraesthesia of the hand during pregnancy has increased in recent years, probably as a result of the recognition of the carpal-tunnel syndrome. Wilkinson (1960) has produced some evidence that during pregnancy compression of the median nerve in the carpal tunnel is due to excessive fluid retention, and McCallum (1959) and Wood (1959) have successfully treated this condition with oral diuretics.

An investigation has been made into the cause of sensory disturbances in the hand during pregnancy and their relationship to excessive fluid retention. Twenty-three patients who attended the antenatal clinics of Queen Charlotte's Hospital during 1959 and 1960 and who complained of symptoms in the hand were selected for the study. Four patients with cramps in the fingers alone were excluded from the series.

Clinical Findings

The time of onset of symptoms varied from the 20th to the 38th week of pregnancy, and in two patients with the carpal-tunnel syndrome the symptoms began in the puerperium. Pain, numbness, and tingling were the most frequent symptoms, and their most common site corresponded with the distribution of the sensory branches of the median nerve (Table I).

TABLE I.—*Site of Sensory Symptoms in the Hand*

Site	No. of Patients
Median-nerve distribution	12
Four fingers ± thumb	10
Inside of forearm and little finger	1

A diagnosis of the carpal-tunnel syndrome was made in 12 patients; the symptoms involved the sensory distribution of the median nerve to the hand and fingers in all cases, and pain was referred to the forearm in seven of them. Only 2 of the 12 patients had symptoms relating to all the branches of the median nerve in the hand. Sensation in the fingers was diminished in five patients and weakness of the hand was present in two. Wasting of the thenar eminence was detected in one patient.

Ten patients had symptoms in the four fingers of one or both hands, the thumb also being affected in eight

of them. This syndrome differed from the carpal-tunnel syndrome in that the little finger was always involved; in addition, the symptoms were sometimes maximal in the little and ring fingers, and pain was referred to the forearm in only one. Sensation in the fingers was diminished in six, but none of the patients complained of weakness of the hand.

A comparison of the clinical features of the carpal-tunnel syndrome and the syndrome affecting the four fingers is shown in Table II. In all these patients, examination of the cervical spine and muscle reflexes of the arm revealed no abnormality. *X*-ray examination of the cervical spine and thoracic outlet was normal in all except one patient who had a cervical rib on the right side and a carpal-tunnel syndrome in the left hand.

TABLE II.—*Clinical Features of Both the Carpal-tunnel and the Four-finger Syndrome in Pregnancy*

	Carpal-tunnel Syndrome	Four-finger Syndrome
No. of cases	12	10
Average time of onset	31st week	28th week
Symptoms:		
Thumb	2	8
Index, middle, and ring fingers	12	10
Little finger	0	10
Forearm	7	1
Weakness of hand	2	0
Finger oedema	10	10
Associated symptoms in leg	5	8

In addition to the sensory disturbance of the hand, approximately one-half of the patients (13/23) had symptoms in the leg; eight had cramps, three sciatica, and two meralgia paraesthetica.

Fluid Retention.—Oedema of the fingers was present in all the patients but two, one of whom developed a carpal-tunnel syndrome during the puerperium. The ankles were swollen in 14 patients; 10 of these had symptoms in the legs.

Although there is a wide variation in the gain in weight during normal pregnancy, Chesley (1944) estimated that the average gain during the second and third trimesters was 1 lb. (450 g.) per week. In 9 of the 13 patients who were weighed before the beginning of treatment, the average gain per week was excessive (Table III).

TABLE III.—*Average Weight Gain Per Week of 13 Patients with Either the Carpal-tunnel or the Four-finger Syndrome*

	Average Weight Gain in Pounds per Week							
	<0·5	0·5–	1–	1·5–	2–	2·5–	3–	3·5–3·9
No. of patients	0	1	3	6	2	0	0	1

Treatment

Because patients with sensory symptoms in the hand during pregnancy also had finger oedema, treatment with oral diuretics was tried. A double-blind trial of the oral diuretic hydrochlorothiazide was abandoned because of the persistence of severe symptoms in the first three patients taking the dummy tablets. Subsequently, all patients were given 50 mg. of hydrochlorothiazide ("hydrosaluric") twice a day for one week. Of the 21 patients receiving treatment, 19 were improved or cured (Table IV). In most of them the finger oedema and weight diminished. The failure of the dummy tablets in three patients and the association of fluid loss with the relief of symptoms during treatment with hydrochlorothiazide suggest that diuretics may be effective in patients with the carpal-tunnel and the four-finger syndromes. In addition, if the symptoms recurred after cessation of therapy they were relieved by further treatment with hydrochlorothiazide.

TABLE IV.—*Results of Hydrochlorothiazide Therapy in Patients with the Carpal-tunnel and Four-finger Syndrome*

Symptoms	Carpal-tunnel Syndrome	Four-finger Syndrome
Unchanged	2	0
Diminished	3	2
Cured	7	7

Treatment failed in two patients; one had a carpal-tunnel syndrome during the puerperium with no finger oedema, and the other had gross finger oedema which hydrochlorothiazide did not reduce. Side-effects attributed to the drug were infrequent. One patient had a marked diuresis with a loss in weight of 7 lb. (3.2 kg.) in one week and a feeling of weakness; two other patients complained of vomiting while taking the drug. Although prolonged administration of hydrochlorothiazide was necessary to maintain symptom relief in several patients, they showed no clinical or biochemical evidence of potassium depletion.

Discussion

Sensory symptoms in the hand during pregnancy were most commonly due to the carpal-tunnel and the four-finger syndromes. The findings in the present series support the theory that fluid retention is the main factor producing the carpal-tunnel syndrome in pregnancy. However, cases that occur in the first trimester or puerperium are unlikely to be associated with fluid retention, and excessive or unaccustomed exercise may precipitate the onset of symptoms in these patients.

Sensory disturbance of the four fingers could be caused by a lesion of the digital nerves, the terminal parts of the median and ulnar nerves, or the median nerve alone. Although the median nerve may occasionally supply sensory branches to the little finger, it is unlikely to do this as often as symptoms occur in this digit during pregnancy. The absence of both motor involvement of the hand and referred pain to the forearm suggests that the symptoms are not due to a lesion of the terminal parts of the median and ulnar nerves. Loss of digital nerve function seems the most likely explanation of the sensory disturbance, but until further evidence of the cause of these symptoms is obtained the lesion may best be called "the four-finger syndrome." This syndrome is also associated with excessive fluid retention, which suggests that it may result from either intraneural oedema or nerve compression by swollen soft tissues. There was no clinical or radiological evidence of an abnormality of the cervical spine, the thoracic outlet, or the main peripheral nerves in these cases.

Summary

A study of 23 patients with paraesthesia of the hand in pregnancy is reported. The most common cause of these symptoms is the carpal-tunnel syndrome.

The other common cause of these symptoms is the four-finger syndrome. This differs from the carpal-tunnel syndrome and is probably due to loss of digital nerve function.

Approximately one-half of the patients also have symptoms in the leg.

Excessive fluid retention during pregnancy may precipitate the onset of symptoms in both the carpal-tunnel and the four-finger syndromes.

Hydrochlorothiazide was usually successful in relieving the symptoms.

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PROLONGED BLEEDING-TIME AND A.H.G. DEFICIENCY

A CASE TREATED WITH OESTROGENS

BY

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It is now realized that the haemorrhagic diathesis characterized by a prolonged bleeding-time and a normal platelet count, and variously referred to as von Willebrand's syndrome, pseudohaemophilia, vascular haemophilia, and hereditary thrombopathy, represents a heterogeneous group of disorders. Haemostatic defects described in patients with this condition include abnormal capillary morphology and function (Macfarlane, 1941; Schulman *et al.*, 1955), antihaemophilic globulin (A.H.G.) deficiency (Alexander and Goldstein, 1953; Valberg and Brown, 1958), a deficiency of a haemostatic factor in the 1–0 fraction of plasma (Nilsson *et al.*, 1957), and a morphological or functional abnormality of platelets (Sussman *et al.*, 1952; Braunsteiner and Pakesch, 1956). The finding of the Bridge anticoagulant in the patient described adds yet another to the list.

Although haemorrhage in these patients is not usually serious, fatalities have been recorded (Buchanan and Leavell, 1956; Lavelle, 1957). No long-term treatment has yet proved effective in controlling the bleeding tendency. For this reason the following case of a severely affected patient is reported, as treatment with oestrogens appeared to prevent the onset of spontaneous bleeding.

Case Report

A 12-year-old girl was first admitted to hospital in 1950, when 18 months old, because of uncontrollable bleeding from a laceration of the lower lip. Her mother said the child had always tended to bruise easily. Pallor and numerous bruises on both legs were the only abnormal findings noted on examination. Bleeding stopped after local haemostatic therapy and a transfusion of 1 pint (570 ml.) of stored blood.

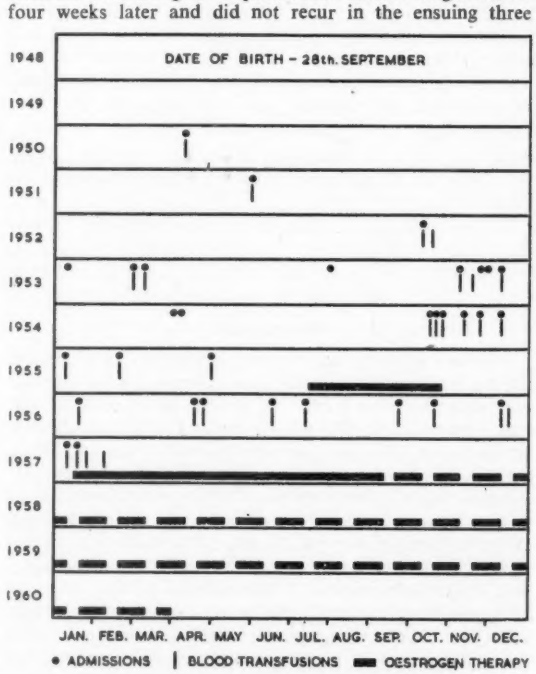
She remained well until readmitted to hospital 14 months later because of profuse bleeding from the nasopharynx after an injury with the handle of a toy spade. Her haemoglobin was 5.5 g./100 ml. She was transfused with 2 pints (1,140 ml.) of fresh whole blood. Haematological investigations showed a bleeding-time in excess of 30 minutes, clotting-time 3½ minutes, platelet count 250,000/c.mm., and a positive capillary fragility test (see Table).

No further bleeding episodes occurred until October 13, 1952, when the child was readmitted to hospital in a shocked condition after a massive spontaneous haematemesis. Bleeding ceased after the transfusion of 3 pints (1.7 litres) of stored blood. Her haemoglobin after transfusion was 10.9 g./100 ml. As additional therapy she was given a five-weeks course of cortisone (100 mg./24 hours), starting on October 17, 1952.

Between this episode in October, 1952, and May, 1955, she was admitted to hospital on 19 occasions because of spontaneous haematemeses. On 13 of these the bleeding was severe enough to require treatment by blood transfusion (see Fig.); a total of 28 pints (15.9 litres) was given. Ecchymoses were always in evidence. She had no haemarthroses.

Between May 7, 1955, and January 21, 1956, the patient was free from bleeding episodes. During this period she was given a 13-weeks course of stilboestrol, 10 mg. daily, starting on July 14, 1955.

Severe haematemeses recurred in January, 1956, and during the next 12 months she was admitted to hospital nine times. On each occasion she required blood transfusions to correct the loss of blood and peripheral vascular collapse resulting from copious gastro-intestinal haemorrhage (see Fig.); 22 pints (12.5 litres) were given. At this time her condition gave rise to increasing concern not only because the haematemeses were becoming more severe but also because the setting-up of blood transfusions was becoming increasingly difficult. On January 11, 1957, she was restarted on oestrogens. Spontaneous haemorrhages ceased four weeks later and did not recur in the ensuing three



Summary of patient's hospital admissions and treatment.

years and two months, during which she was given oestrogens. Therapy was started with stilboestrol 10 mg. twice daily; after one week this dose was gradually reduced to 1 mg. a day by April 27, and 0.25 mg. a day by June 8. The dose was altered on August 22 to intermittent treatment with 0.25 mg. daily for 20 days followed by a 10-day interval off treatment. After 12 months dienoestrol 0.5 mg. a day was substituted for stilboestrol. Between December, 1959, and April 1960, she started to have regular menstruation, and oestrogen therapy was discontinued in March, 1960. She has continued to have a monthly menstrual cycle without excessive loss and has had no bleeding episode during the 16 months since discontinuing oestrogen therapy.

Though she was clinically well, there was no obvious shortening of the bleeding-time while on oestrogens. The only side-effects produced by oestrogens were in breast development, pigmentation of areolae, and a growth spurt of 8 in. (20 cm.) in the three years; she had no vaginal bleeding on the intermittent course of oestrogens.

The results of haematological investigations carried out on this patient are shown in the Table. In addition, the following investigations were performed at various times with negative results: bone-marrow examination, oesophagoscopy, gastroscopy, and radiological examination with a barium meal and follow-through. A family history of bleeding was not elicited. Haematological investigations on the patient's parents and brother showed no abnormality and in particular no decrease in A.H.G.

Discussion

The results of laboratory studies show that this patient suffered from a haemorrhagic disorder with a prolonged bleeding-time and a deficiency of A.H.G. Initial studies, undertaken before the start of oestrogen treatment, also indicated the existence of a qualitative platelet abnormality. In addition, an anticoagulant of the Bridge type was demonstrated in the patient's plasma. This latter finding has not been previously reported, and is contrary to the observations of Wilkinson *et al.* (1958), who found no Bridge anticoagulant in the plasma of three patients suffering from von Willebrand's syndrome and an A.H.G. deficiency.

A positive family history in these cases is usual with the trait inherited as an autosomal dominant (Nilsson *et al.*, 1957; Quick, 1959). Nilsson *et al.* (1957) investigated six families with members affected with von Willebrand's syndrome and an associated A.H.G. deficiency. In every instance they were able to demonstrate a reduced A.H.G. level in one or other parent of an affected child even though some were clinically unaffected. In our case, however, there was no family history of a similar disorder and no haemostatic defect could be demonstrated in the patient's parents or brother.

This patient showed the clinical features of bruising, persistent bleeding from wounds, and spontaneous gastro-intestinal haemorrhages. Haemarthroses did not occur, which is of interest in view of the very low A.H.G. values recorded (1.2 and 2.6%) and the presence of Bridge anticoagulant in the plasma.

The reported incidence of spontaneous gastro-intestinal bleeding in patients with von Willebrand's syndrome varies from 17% (Buchanan and Leavell, 1956) to 50% (Horler and Witts, 1958). The mortality would appear to be higher among patients with this symptom. Apart from the patient under discussion, one of us (B. N.) has investigated 10 patients with von Willebrand's syndrome associated with an A.H.G. deficiency; two of four who suffered from spontaneous gastro-intestinal haemorrhage died.

Treatment of this disease is unsatisfactory and there is as yet no known effective means of permanently controlling the bleeding tendency in these patients. Nilsson *et al.* (1959) have reported success in controlling the haemorrhage of acute episodes by injections of plasma fraction 1–0, which corrected the bleeding-time and increased the A.H.G. level for 24–48 hours. This therapy, however, is not as yet suitable for long-term use. Cortisone is of questionable value, though some encouraging reports have been published (Jacobson, 1953; McIlvanie, 1958). In our patient, cortisone, when tried in 1952, was thought to have been of no value, but in retrospect the prescribed course of treatment cannot be regarded as constituting an adequate trial.

Oestrogens were originally given to our patient because of the report of Guichard and Revol (1949). These authors reported a temporary remission in a male patient with a similar disorder on treatment with oestrogen. In our patient an initial 13-weeks course of stilboestrol coincided with a period of eight and a half months during which she had no spontaneous gastro-intestinal bleeding. As naturally occurring remissions are a feature of this disorder an accurate assessment of any form of treatment is difficult. None the less, it would appear more than coincidental that when oestrogen therapy was repeated 18 months later spontaneous gastro-intestinal haemorrhages ceased throughout the period of treatment (three and a quarter years) with the exception of the first month. This was in marked contrast to the experience of the preceding four and a quarter years, during which the child was admitted to hospital on 29 occasions and received 26 blood transfusions because of gastro-intestinal bleeding (see Fig.).

Although clinical improvement was obvious the prolonged bleeding-time was not altered. A beneficial effect of oestrogen is not necessarily ruled out by this finding, as the bleeding tendency in this disease does not

Results of Haematological Investigations

	1951	1952–5	1958	1959	1960
Bleeding-time (min.)	30+	30+	30+	18+	
Hess's test	Positive	Negative	Positive	Negative	—
Morphology of capillaries	Normal	Normal	Normal	—	—
Platelet count (per c.mm.)	250,000	171,000	292,000	198,000	—
Platelet morphology	Normal	Normal	Normal	Normal	Normal
Platelet study	—	Patient's platelets did not restore to normal the consumption of prothrombin in normal platelet-poor plasma*	—	—	Patient's platelets restored to normal the consumption of prothrombin in normal platelet-poor plasma
Coagulation time (min.)	3½ capillary	—	9	10	10
Clot retraction	—	—	Normal	Normal	Normal
Prothrombin time (sec.)	—	—	11	12	12
Serum prothrombin activity (%)	—	—	15	20	40
Thromboplastin generation test	—	—	—	Abnormal†	Abnormal†
A.H.G. (%)	—	—	1·2	2·6	—
Bridge anticoagulant	—	—	—	—	Present
Plasma fibrinogen	—	—	182	—	—
Electrophoresis	—	—	Normal	Normal	—

* Details of these studies have been previously reported (Neely *et al.*, 1955).
† Corrected by substituting normal adsorbed plasma for patient's plasma in the incubation mixture.

always parallel the bleeding-time (Irvine and Jones, 1957). Although there is clinical evidence that oestrogens may promote haemostasis (Jacobson, 1954) the actual mechanism of action is unknown. It has been suggested that oestrogens may influence the production of prothrombin and factor V (Johnson, 1957), capillary permeability (Wells, 1958), or platelet function (Frazer, 1958). It is of interest that studies of platelet function showed a qualitative defect when performed in 1954 before the onset of oestrogen therapy (Neely *et al.*, 1955). When next repeated in 1960, three months after discontinuing oestrogens and more than three and a half years since the patient's last spontaneous gastro-intestinal haemorrhage, no functional abnormality of platelets could be demonstrated.

If the oestrogen effect is limited to the correction of a single defect it is obvious that oestrogens will not be of value in all cases, as von Willebrand's syndrome includes different combinations of haemostatic defects. None the less, in view of the seriousness of gastro-intestinal bleeding in these patients and of the probable life-saving effect noted in our patient it would appear that this therapy should be tried in such cases.

Summary

A case is described of a girl with a prolonged bleeding-time associated with a severe deficiency of A.H.G. Bridge anticoagulant, which has previously been reported as absent in patients with von Willebrand's syndrome, was present in her plasma.

Between the ages of 4 and 8¼ years this child was admitted to hospital on 29 occasions because of massive spontaneous haematemeses; she required 26 transfusions and received 53 pints (30 litres) of blood. She was then treated with oestrogens. With the exception of the first month she had no gastro-intestinal bleeding throughout the three and a quarter years of treatment.

It is suggested that prolonged oestrogen therapy may be of value in some patients with this condition.

Our thanks are due to Professor F. M. B. Allen for permission to publish this case and to Dr. M. G. Nelson for advice in the preparation of this paper.

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OBSTRUCTION OF CENTRAL RETINAL ARTERY ASSOCIATED WITH CHOREA

BY

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Arterial obstruction of the retina in Sydenham's chorea is of extreme rarity. There have been few references in the literature to its occurrence (Swanzy, 1875; Thomas, 1901; Harms, 1914; Coats, 1914; Knapp, 1918; Langdon, 1925; Milnes Bride, 1937), and most of them suggested that the occlusion was due to embolus by a vegetation from a heart valve affected by coexistent rheumatic endocarditis. Only one of these reports is later than 1925, and in making this suggestion they reflect one of the opinions held at that time regarding the aetiology of chorea.

The embolic theory of the causation of chorea is no longer acceptable, and it is now obvious that there is no pathology common to all cases of chorea. In some cases inflammatory changes predominate, in many studies degenerative changes are the only finding, and in some vascular changes occur as the principal feature. The variation in appearances from case to case is so wide as to suggest that chorea is not a disease but a syndrome.

A case has recently been observed in which the association of a retinal artery occlusion with symptoms of chorea suggested a common vascular pathology to both phenomena. It is here reported as an interesting rarity and as possibly making some minor contribution to the pathology of chorea.

Case Report

A single woman aged 20, employed as a clerk, attended hospital on February 7, 1958. She stated that on coming down to breakfast at 7.45 a.m. her left eye became completely and suddenly blind. After what seemed a few minutes there was some improvement, and by the time she reached hospital she found that she could see the upper half of objects. There was no pain associated with the loss of vision.

On examination of the eyes her visual acuity was found to be right, 6/6; left, hand movements. The right eye showed no abnormality, with a full visual field. The left eye showed an obstruction of the superior branch of the central retinal artery, with oedema above the macula which stood out as a "cherry spot." There was a loss of the whole lower visual field.

Immediate retrobulbar injection of carbachol 0.25 mg. was given, and after general examination had shown no abnormal finding this was followed by a retrobulbar injection of tolazoline hydrochloride B.P.C. 25 mg. Oral treatment was continued in a dosage of 50 mg. q.i.d. The patient was admitted for investigation and treatment.

After the first retrobulbar injection the disk was examined more closely; overlying the bifurcation of the main trunk of the central artery was a tuft of diaphanous material appearing rather like an early retinitis proliferans, and, above this, fragmentation was seen in the blood column of the superior temporal branch.

The next day the tuft was smaller, the upper vessels were wider in calibre but still narrower than those below, and

there was no longer any fragmentation of the blood column. Pulsation could not be felt in the superior vessels. Subjectively, her vision was further improved, and on confrontation her peripheral field was partly recovered in all meridians, but a lower altitudinal scotoma persisted.

On February 10 it was noted that there was no past history of serious ill-health or previous history of acute rheumatism. Pyrexia to 99° F. (37.2° C.) had been recorded on two occasions since admission. The skin was warm and moist; the mitral first sound was duplicated, but otherwise clinical examination showed nothing abnormal. The blood-pressure was 120/80. The blood count was within normal limits and the sedimentation rate was 7 mm./hour (Wintrobe).

Embolism from a vegetation of bacterial endocarditis could not be excluded at that stage, and she was transferred to a medical ward for investigation. The white-cell count remained within normal limits and the erythrocyte sedimentation rate at a normal level. Three blood cultures were negative. *X*-ray examination of the chest and screening showed no abnormality.

She remained under in-patient observation without treatment until February 27, when it was noted that she had developed hypermotility, grimacing, and purposeless movements of the limbs; all reflexes were brisk, sustained knee-jerks were present, the typical hyperextension of the outstretched fingers appeared, and the hands when raised above the head were everted. The appearances were typically those of Sydenham's chorea. As these phenomena might have been fleeting, and as the diagnosis of chorea was not susceptible to proof by objective tests, clinical confirmation seemed desirable to exclude observer error. She was therefore seen in consultation by Dr. M. E. Disney, consultant paediatrician, and Dr. E. R. Bickerstaff, consultant neurologist, who concurred in the diagnosis of chorea.

She was treated with sodium salicylate 12 g. daily, with serum salicylate studies on alternate days. By March 15 she was much improved, and by March 27 the signs of chorea had disappeared. The erythrocyte sedimentation rate and electrocardiogram had remained normal throughout. There was at no time evidence of carditis.

She was discharged from hospital on March 31 and from that date has received sulphadimidine 1 g. daily. A short-term fever of undetermined origin occurred on April 22, 1959, and persisted for four days; otherwise the patient has remained well. No evidence of a cardiac lesion has appeared.

Vision.—When the eyes were re-examined on June 13 the fundus appearance was normal apart from reduced calibre of the superior branch of the central artery (see Figure). She still showed an altitudinal scotoma, with impairment of the lower peripheral field. Her vision had improved to 6/36 (6/24 when fixing eccentrically). Subsequently further improvement of acuity took place to 6/5 with reduction in the size of the scotoma, which, however, still split the central field horizontally.

Review of Literature

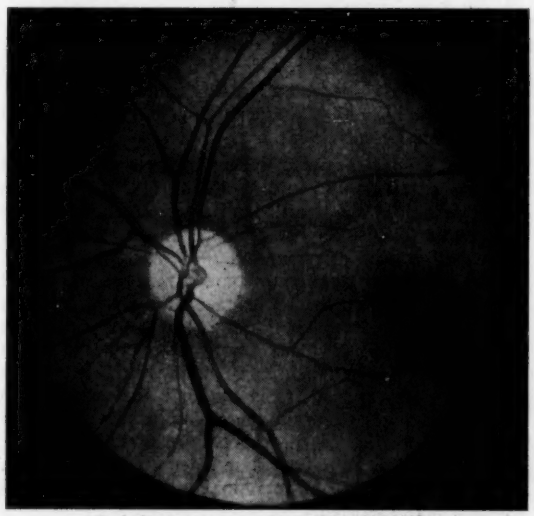
Langdon (1925) refers to 11 reported cases of embolism of the central retinal artery among the ocular complications of chorea (Swanzy, 1875; Thomas, 1901; Harms, 1914; Coats, 1914; Knapp, 1918). Not all of these were fully described, but all cases showed a sudden loss of vision in one eye of a patient with established chorea. The first examination of the eye had been made in most cases after an interval of a few hours. In a few cases the patient's eyes were examined after a longer interval up to 10 years; in the early cases the affected artery was found to be "small, pale but not quite empty, the retina hazy around the disk and a cherry spot at the macula"; "normal retinal vessels except the inferior temporal artery, which had collapsed; haze of the retina and a 'cherry red' spot at the macula"; "a small plug at the bifurcation of the superior and inferior arteries, the arteries themselves being small, the veins about normal in size, and a cloud in the temporal portion of the retina, with the macula spot showing dark red." The later findings in most were of complete optic atrophy, as one would expect in total blindness from occlusion persisting for any length of time.

The case described by Swanzy (1875) and quoted by Langdon (1925) was most interesting, because the original occlusion did not appear to be complete, although the eye at first examination was totally blind. Both the chorea and the vision had improved three weeks later, when the patient was able to count fingers at 5 in (12.5 cm.). The disk gradually paled and the inferior nasal branch of the artery collapsed, later to have its blood column return. No cardiac disease could be found in this case. The chorea coincided in its onset with the blindness and affected particularly the left arm and leg. Swanzy's case differed from the other reported cases in these respects—the almost simultaneous onset of the chorea and blindness, the incomplete nature of the obstruction, and the partial recovery of vision. In none of the other reported cases was there any visual recovery.

In addition to these cases collected by Langdon, which dated from 1875 to 1924, we have traced only one other case report. Milnes Bride (1937) reported a case which he thought to be due to embolism in association with chorea. No details were given of the findings on general examination, but he implied that no heart disease was found.

Discussion

It was felt by earlier authors that most of these retinal arterial obstructions occurring in the course of chorea were due to emboli, although this had never had general acceptance. Thomas (1901) maintained that emboli affecting the corpora striata were the most probable cause of chorea, but pointed out that few cases of chorea coming to necropsy showed any evidence of emboli and threw doubt on the embolic theory without offering any other explanation. Arnold Knapp's (1918) case of retinal artery obstruction and chorea also showed the presence of endocarditis, and Knapp



Left fundus appearance on June 13, 1958.

suggested that the appearance of this retinal embolism supported the theory which held chorea to be of embolic origin. Langdon (1925) concluded also that his case was due to embolism.

It is noteworthy that out of five cases of retinal arterial obstruction where the state of the heart was reported (Swanzy, 1875 ; Knapp, 1918 ; Langdon, 1925 ; Milnes Bride, 1937) two—those of Swanzy and Milnes Bride—were said to show no evidence of endocarditis. Our case falls into the latter group.

The theory that chorea was due to multiple emboli never enjoyed complete acceptance and now has no support. Greenfield and Wolfsohn (1922) quoted 15 references from the earlier literature noting Kirkes and Hughlings Jackson as expounding the " embolic theory " of chorea and Bastian as offering a " thrombotic theory," " the corpora striata and adjacent parts being the seat of a subacute inflammation characterized in part by the production of multiple minute thromboses." Other authors were quoted as reporting changes principally in the architecture and staining properties of the neurones. There was so much variety from case to case in the pathological changes observed by the authors quoted by them that Greenfield and Wolfsohn " concluded from a study of the above that there was still much to be written about the pathology of the disease." They described a necropsy study of their own on a female patient aged 7 years who died of acute chorea and in whom vegetations were found on the mitral and aortic valves. Vascular changes were present everywhere in the brain. Many of the cortical vessels had undergone thrombosis and some of the smaller vessels showed plugging by clumps of leucocytes. Many of the capillaries showed proliferation of their endothelial lining, and outside these there were in many places chains of small round cells.

They concluded that if emboli did occur in chorea these could not be the cause of symptoms since (1) chorea did not occur in ulcerative endocarditis, nor did the symptoms of cerebral embolism correspond to chorea ; (2) many cases of chorea occurred where there was no disease of the heart valves and therefore no source for the hypothetical emboli ; and (3) it seemed impossible to believe that the symptoms produced by an embolism would have yielded so rapidly to treatment as those of acute chorea frequently did.

Subsequent histological studies have been few. We have traced two cases reported by Buchanan, Walker, and Case (1942), one by Bauer, Riley, and Cohen (1950), one by Colony and Malmud (1956), and two reported by Maurice Lessof (1958).

These scattered, more recent reports confirm the findings of Greenfield and Wolfsohn (1922) that there is no pathology common to all cases of chorea. The arguments against an embolic pathology advanced by them still appear relevant, but these arguments would not be valid when applied to a concurrent retinal arterial occlusion. In fact, the occurrence of a fibrin embolus seems a possible explanation for this event, although this explanation would be more acceptable in those cases where acute rheumatic endocarditis had been detected. However, there is evidence that widespread vascular changes occur in the brain in some cases of chorea, appearing as thromboses or endothelial proliferation. It is felt that these phenomena cannot be excluded as causes of the retinal arterial occlusion in the case here reported.

Summary

A case of retinal arterial obstruction is reported in which chorea was subsequently observed.

Twelve other cases of retinal arterial occlusion in association with chorea have been traced in the literature.

Possible causes for this disorder are discussed.

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Medical Memoranda

Protein-secreting Tumour of Stomach: Severe Hypoproteinaemia Cured by Removal of Gastric Polyp

Severe hypoproteinaemia is always a sign of disease, in some cases due to easily recognized external loss of protein (nephrosis, burns, bleeding), in others to a reduced production (liver diseases and chronic infections) or increased internal breakdown of albumin (fever, A.C.T.H. therapy).

Recent investigations have shown that idiopathic hypoproteinaemia, too, is not a disease *sui generis*. In all the studied cases the hypoproteinaemia was due to loss of protein (primarily albumin) into the lumen of the gastro-intestinal tract (Gordon, 1959 ; Schwartz and Jarnum, 1959 ; Young *et al.*, 1959 ; Gross *et al.*, 1960 ; Jarnum and Petersen, 1961). Here the proteins are digested by the enzymes, and, as the liver is unable to increase its albumin production sufficiently, hypoproteinaemia results. This so-called " protein-losing gastro-enteropathy " (*Lancet*, 1959) has proved to be associated with different diseases: hypertrophic gastritis, gastric carcinoma, granulomatous diseases of the small intestine and mesentery, and regional enteritis. The loss of protein can even take place through a small intestine without any striking gross or microscopical changes.

A case of excessive hypoproteinaemia caused by gastro-intestinal loss of protein from a gastric tumour is here reported.

CASE HISTORY

A 73-year-old man was admitted to the neurological department, Copenhagen County Hospital, Glostrup, because of a suspicion of brain tumour. He had had no serious illnesses previously, but two years before admission oedema of feet and legs started, gradually spreading upwards. The oedema had not caused any great discomfort. He had eaten ordinary food and had not had any gastro-intestinal complaints whatsoever. Marked exacerbation of the leg oedema, enlargement of his girth, and dizziness and

headache followed influenza A 18 months before admission. As a neurological examination failed to reveal any abnormality, he was transferred to medical department F.

Physical examination showed severe oedema of the legs, abdomen, and back as far as the scapulae, severe ascites, and right-sided hydrothorax.

Laboratory Findings.—Hb, 10.1 g./100 ml.; red cells, 3,050,000/c.mm.; weight, 63.1 kg.; E.S.R., 6 and 3 mm./hr. Faeces: negative benzidine reaction. Thymol test, zinc sulphate, alkaline phosphatase, serum cholesterol, and serum creatinine were normal. Urine: no albumin. Serum protein, 3.1 g./100 ml.; serum albumin, 1 g./100 ml. Fasting gastric juice: + free acid and + free albumin on electrophoresis.

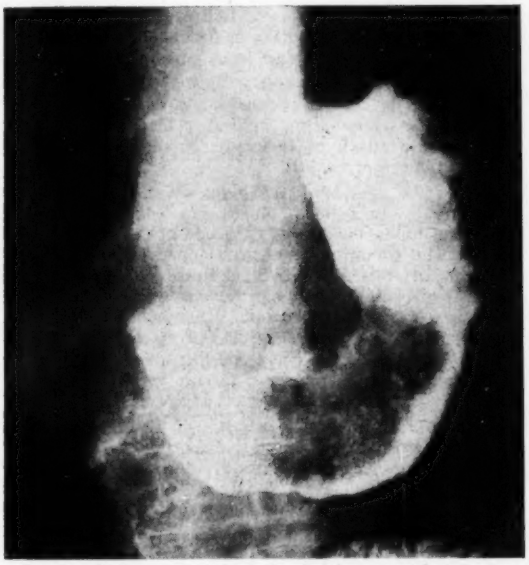

FIG. 1.—Radiograph of stomach, showing a gastric tumour.

X-ray Studies.—Chest: right-sided hydrothorax and atelectasis of the right lower lobe. Stomach: a tumour in the middle part of the stomach (see Fig. 1), presumably situated on the posterior wall of the body of the stomach. Fundus and pyloric region normal. Duodenum and small intestine: no abnormality.

The albumin turnover was studied by ^{131}I albumin, using the method of Pearson *et al.* (1958). The degradation constant was distinctly increased for circulating albumin (19.8% as compared with the normal range of 5.6–14.4%). The faecal excretion of ^{131}I activity was followed for five days, during which it was greatly increased (Schwartz and Jarnum, 1961). Later, a ^{131}I-polyvinylpyrrolidone test was carried out. This also showed an abnormally high faecal excretion (see Table).

The severe and otherwise unexplained hypoproteinaemia combined with definite evidence of a considerable gastro-intestinal loss of protein directly indicated the gastric tumour as the site of the leakage. There were no signs of inoperability.

Total Serum Protein, Serum Albumin, and Gastro-intestinal Protein Loss Before and After Removal of Protein-secreting Gastric Tumour

	Before Operation	After Operation	Normal
Total serum proteins (g./100 ml.)	3·1	7·3	5·9 –8·1
Serum albumin (g./100 ml.) ..	1·0	4·7	3·8 –5·1
Faecal loss of activity in 5 days after ^{131}I albumin	1·7%	—	0·0 –0·39%
Faecal loss of activity in 5 days after ^{131}I-P.V.P.	3·3%	0·16%	0·03–1·01%

After several transfusions of plasma, albumin, and blood —during which the patient lost 13 kg.—the plasma proteins and haemoglobin returned to normal and laparotomy was performed.

The liver and intestines were normal. There was no ascites. Since, furthermore, there were no gross signs of nodal involvement and the tumour was well defined, subtotal gastric resection by the Hofmeister method was carried out. The removed tumour (Fig. 2) was irregular in shape, polypous, well defined from the gastric wall, and had a wide base with raised edges. Its size was 5.5 by 3 by 2.5 cm. The cut surface was greyish, firm, and elastic.

Microscopical Examination (Fig. 3).—The larger part of the polypous tumour consisted of very densely arranged glands lined with simple columnar epithelium. There was moderate infiltration with granulocytes, plasma cells, and lymphocytes. In some places glandular tissue infiltrated the muscles, and in several sites there were dilated lymph spaces with solid clusters of dedifferentiated glandular epithelium. Diagnosis: mucous polyp of the stomach (adenoma) with patches of carcinomatous development (E. Bredahl).

Radioactivity Study of Tumour Tissue and Gastric Tissue.—During the operation ^{131}I albumin was injected intravenously. From the removed operative specimen tissues were at once obtained for measurement of radioactivity in the tumour and in the normal mucosa of the body of the stomach. The activity in the tissues was slight, while in the tumour tissue it was twice that in normal mucosa. The results indicate that the tumour contained much more albumin than the normal gastric mucosa.

The post-operative course was entirely uneventful and the patient was discharged in good health at the end of two weeks.

At a follow-up study four months later he was feeling well in every way. The oedema had completely vanished after the operation. Serum protein and the ^{131}I-P.V.P. test (see Table) were normal.

COMMENT

The present case is of particular interest as the patient's actual disease—a gastric tumour—manifested itself exclusively by hypoproteinaemic oedema—that is, a case of "idiopathic" hypoproteinaemia.

The architecture of the polypous gastric tumour was very like that of the mucous membrane in "giant"

FIG. 2.—Resected part of stomach, showing the gastric polyp. Pyloric part on right.

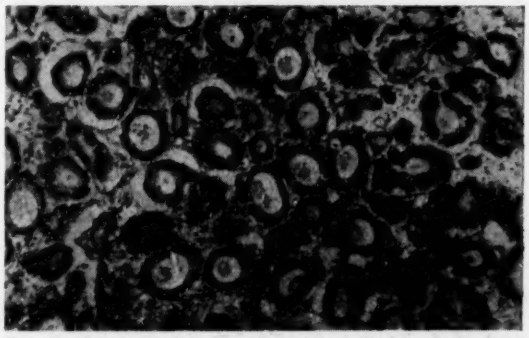

FIG. 3.—Adenoma with several densely arranged glands lined with cuboidal-columnar epithelium.

hypertrophic gastritis (Menetrier's disease), in which hypoproteinaemia and a considerable protein loss in the stomach (Schwartz and Jarnum, 1959) is very common. It seems likely that in both cases the loss of protein occurs through secretion of protein-containing fluid into the gastric lumen. In actual cancer of the stomach, hypoalbuminaemia is a common finding and is due, at least partially, to gastro-intestinal loss of protein (Jarnum and Schwartz, 1960).

A conclusion to be drawn from our case is that the gastro-intestinal tract must be examined in all obscure cases of hypoproteinaemia.

This study was supported by grants from the Danish State Research Foundation and the King Christian X Foundation. We thank Dr. R. S. Gordon for a generous supply of ^{131}I-labelled polyvinylpyrrolidone.

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Recurrent Rheumatic Chorea and Optic Atrophy after Occlusion of Central Retinal Artery

The following case is presented to illustrate the association of rheumatic chorea and C.R.A. occlusion in the absence of clinical evidence of carditis.

The patient, a 21-year-old married woman, was admitted to hospital at the beginning of July, 1960, suffering from severe chorea gravidarum. She was in the 23rd week of her second pregnancy and had felt nervous, and had been noticed to be excessively restless, for about two months. She had suffered from mild breathlessness on exertion since childhood, but this was no worse at the time of admission. Her left wrist had been swollen and painful for one week and she complained of a crop of ulcers in her mouth. Foetal movements had been felt for three weeks. Her right eye had been blind since sudden loss of vision in 1957. She had a history of several attacks of acute rheumatism and rheumatic chorea since childhood (see below). One of her sisters had died of acute rheumatism at the age of 7½ years, and a brother had had erythema nodosum as a child. The remainder of her family were healthy.

On admission the patient showed gross choreiform movements of the face, hands, and legs, with some dysarthria, and had a slight, painful swelling of the left wrist and a crop of aphthous ulcers. She was clinically in the 23rd week of a normal pregnancy. The pulse was 80–100 and B.P. 110/70. There was slight clinical cardiac enlargement and a loud apical systolic bruit transmitted up the left sternal border, where it was accompanied by an early diastolic third sound. The second sound was closely split at the base.

The visual acuities were not accurately assessed on admission, but refraction on recovery from the chorea revealed that right vision was reduced to vague hand movements and perception of light in the temporal and inferior fields only. The left vision was improved from 6/60 to 6/6 with $+4.0/+0.50\times90°$. The pupils were equal in size but the right direct and left consensual light reflexes were diminished, the left direct and right consensual reflexes being normal. Fundal examination revealed bilateral hypermetropia and right optic atrophy. The retinal vessels were equal in size in the two eyes and of normal calibre, allowance being made for the hypermetropia.

Nothing significant was found on investigation other than a raised E.S.R. of 54 mm. in one hour (Westergren). The chorea was relieved by bed rest, sedation with phenobarbitone, and full doses of salicylates. The wrist became free from pain and the swelling subsided.

PAST HISTORY

I am grateful to Professor C. B. Perry, of Bristol University, and Mr. B. J. Bowden, of the Bristol Eye Hospital, for supplying the following details of the patient's past medical history and for permitting me to make use of them.

December, 1943 (aged 5 years): Attack of acute rheumatism; no clinical evidence of carditis; 1948: attack of rheumatic chorea; no clinical evidence of carditis; 1954: further attack of rheumatic chorea, again with no clinical evidence of carditis.

March, 1957: Sudden loss of right vision, when seen three days later by an ophthalmologist she was found to have the typical fundal changes of occlusion of the central retinal artery. The condition failed to respond to a retrobulbar injection of tolazoline hydrochloride. A presumptive diagnosis of embolism of the artery was made, though again no clinical evidence of carditis or other embolic phenomena was found. The patient gave a history, at this time, of periodic attacks of transient visual loss, affecting either eye for about a minute at a time, for six years, occurring as often as twice a day or at intervals of several weeks.

October, 1958: Normal delivery of first child after a normal pregnancy, though the patient thinks in retrospect she may have been rather restless during this pregnancy also.

January, 1960: Professor Perry discovered a loud apical systolic murmur for the first time.

COMMENT

The visual loss in the above case did not occur during an attack of chorea, but the rarity of C.R.A. occlusion in a patient of her age (18 years) points to an aetiological association of the condition and her rheumatic diathesis.

The most likely cause of the arterial occlusion would be embolism, but several factors weigh against this possibility: (1) the complete absence of clinical evidence of any form of carditis until almost three years after the visual loss, (2) the absence at the time of the arterial occlusion of other signs of embolic phenomena, and (3) the history of transient attacks of visual loss, culminating in the right C.R.A. occlusion, for a period of six years. The last factor points to these being attacks of spasm of the central retinal artery possibly associated with local arterial disease rather than multiple emboli, as recovery of vision between the attacks was said to be complete.

I thank the Director-General of Medical Services, Royal Air Force, for permission to publish details of this case.

G. S. WILLETTS, M.B., D.O.
Flight Lieutenant, R.A.F.

A new British Standard specification for anti-static rubber flooring (B.S.3398) has recently been issued. Copies may be obtained from the British Standards Institution, Sales Branch, 2 Park Street, London W.1. (Price 4s. each, postage extra to non-subscribers.)

Reviews

SENSORY DEPRIVATION

Sensory Deprivation. A Symposium held at Harvard Medical School. Edited by Philip Solomon, M.D., Philip E. Kubzansky, Ph.D., P. Herbert Leiderman, M.D., Jack H. Mendelson, M.D., Richard Trumbull, Ph.D., and Donald Wexler, M.D. (Pp. 262+xviii. 46s.) Cambridge, Mass.: Harvard University Press. 1961.

Impetus was given to the first studies in the field of sensory deprivation by the disturbing phenomena of brain-washing and by the psychological problems of space flight. Sensory deprivation—meaning the elimination or reduction of sensation from vision, hearing, and touch—lies in an unstudied no-man's-land between the closely related sciences of neurophysiology, experimental psychology, and psychiatry, and so is bound to pose novel problems for research. Questions about the nature of perception and reality, consciousness and attention, which have been riddles for philosophers throughout the centuries, are now acquiring fresh meaning. This book, the report of a symposium held at Harvard Medical School in 1958, gives an excellent survey of the trends in this field of research, which is yet barely ten years old.

The study starts from various methods of reducing sensory stimulation and measuring the responses in human volunteers and in animals. The results are subject to the usual errors in biological experiments and particularly to the individual variation between subjects. The personality of volunteers and their previous conditioning to the experimental situation have probably not yet been adequately examined.

It is now well known that aberrations in thinking and disturbances of behaviour occur under conditions of sensory deprivation. Yet the explanation of these changes is far from clear, and each contributor to this symposium discusses the mechanism in terms of his own science, none of these mechanisms so far being susceptible of proof. The brain, neurophysiologically considered, seems so much more than a computer accepting and analysing information, in that it is to a considerable extent self-stimulating, providing some of its own information, and has complex neural mechanisms underlying alertness and attentiveness. On the basis of visual, auditory, and kinaesthetic clues, the brain seems to impose a structure upon the organism's environment by a process of learning. This process seems to hold in check aberrant tendencies in the perceptual process, which become apparent after sensory deprivation. On the other hand sensory deprivation is seen in psychoanalytic terms as an analogue of the couch situation where attention is withdrawn from outside influences and focuses on the therapist (the experimenter). Following the establishment of the subject's dependence on the experimenter "regression" occurs. In the field of experimental psychology animal studies have shown that sensory deprivation during rearing is later followed by inadequate responses, both to the stimuli of which the animals were deprived and also to other stimuli. It seems important from the point of view of educational theory that certain intricate adjustments to complex sensory patterns can be acquired only at a certain stage of the organism's development and thereafter the opportunity is lost. In human disease, experiments in sensory deprivation suggest a promising way of studying symptoms which resemble strikingly some of the symptoms of psychotic states.

This symposium is in the nature of an overture; the main body of the work has yet to come.

R. G. BANNISTER.

ACCLIMATIZATION CLASSIC

Physiological Responses to Hot Environments. M.R.C. Special Report Series No. 298. An account of the work done in Singapore, 1948–1953, at the Royal Naval Tropical Research Unit with an appendix on preliminary work done at the National Hospital for Nervous Diseases, London. Compiled by R. K. Macpherson. (Pp. 323+xv. 35s.) London: H.M. Stationery Office. 1960.

This is a detailed and involved account of work done with two main objects: the first was to measure the effects of variations in the several components of environmental stress and to devise an index of these effects; the second was to select one or more measures of physiological strain and to compare the effects of a series of environments on the selected measures, and in doing so to relate the effects of environment to the degree of acclimatization of individuals. This work on these important though difficult objectives had its origin in a request from the Admiralty that a committee should be established among whose terms of reference was the undertaking of investigations on the psychological and physiological aspects of matters affecting the safety and efficiency of Royal Naval personnel. The investigations were carried out by 30 workers between 1948 and 1953, and from the report it is clear that it has been done imaginatively, with great care, and that the highest scientific standards have been set. The excellence of the design of the experiments and the statistical control is outstanding.

It was soon found that the Effective Temperature Scale was unsatisfactory except for assessing comfort in the middle range of environmental stress, and this led to devising a new scale, the Predicted Four-hour Sweat Rate, which was more suitable for defining the accepted upper limit for environmental heat stress. With this scale the results of a wide variety of stresses were measured and the efficiency of different means of acclimatization was assessed. Of particular importance was the finding that artificial acclimatization could greatly improve the ability to withstand heat and that men so acclimatized in London possessed a greater degree of acclimatization than was ordinarily possessed by naval ratings serving in the tropics. The fundamental mechanisms of acclimatization have not been found, but the work forms a step towards their elucidation.

The increase in movement—and sometimes mass movement—of persons to and from tropical regions renders studies of this kind of vital importance to modern living and perhaps to survival. But the book is more than a guide to applied problems, for it also contains valuable contributions to fundamental knowledge. The complexity and the technicalities of the subject make it difficult to read. This, however, does not dim the lustre of what is a classic of its kind which will deservedly become a standard work of reference.

A. W. WOODRUFF.

MEDICINAL CHEMISTRY

Progress in Medicinal Chemistry. Volume 1. Edited by G. P. Ellis, B.Sc., Ph.D., F.R.I.C., and G. B. West, B.Pharm., D.Sc., Ph.D. (Pp. 262+ix; illustrated. 60s.) London: Butterworths. 1961.

From its title this book is evidently written for research workers in pharmaceutical houses, and certainly it should be extremely useful to them. The book is

presented in six sections. Four of these—hypotensive agents, tranquillizers, diuretic drugs, and oral hypoglycaemic drugs—are well worth study by medical men also, for they are written with authority. The sections on diuretic drugs and on oral hypoglycaemic drugs are perhaps the best accounts available at the present time. All have long lists of references.

From the section on tranquillizers, the following sentences deserve quotation: "The reports of clinical experience with meprobamate present a confused picture. Its effect in psychotics appears to be slight, or absent, although a quietening action has been described. There are many reports of the treatment of anxiety and tension states, some favourable, and a similar number unfavourable. In general, the improvement rate is reported to be about 40% and it is probable that the difference between this and the effect which can be produced with a placebo is marginal." A more severe comment on the enormous sums which are known to have been spent in the United States on meprobamate can scarcely be imagined. We may wonder if these sales have made their impression on Mr. Enoch Powell.

The section on antifungal agents is a noble effort, but it consists of indigestible observations which the authors have not been able to piece together into any story. Their account suggests that fungal infections offer a wonderful and probably easy field for basic research.

The one section in the book which is poor is the first. Neither the author, nor indeed the editors of the book, appear to understand what is meant by "screening." They seem to think it is a term equivalent to general pharmacological examination. The first five lines on page 2 indicate this so far as the author is concerned. To "screen" is to sift by passing through a screen (O.E.D.), a screen being an apparatus used in the sifting of grain or coal. Compounds can be "screened" for one particular activity — for example, antimalarial activity. But screening has nothing to do with discovering what properties a substance possesses.

J. H. BURN.

ANTIBIOTICS

Antibiotica. Herkunft, Arten, Eigenschaften. By Professor Dr. Tadeusz Korybski and Professor Dr. Włodzimierz Kuryłowicz. (Pp. 1,105+xix. DM. 130.) Jena: Veb Gustav Fischer Verlag. 1961.

This is the second edition, translated into German, of a treatise on the origin, nature, and properties of the antibiotics, by two members of the Research Institute for Antibiotics in Warsaw. It contains descriptions of some 800 substances, and the fact that this is about twice the number described in the first edition gives an indication of the growth of the subject within the last five years.

The substances are classified according to the organisms by which they are produced. This system of classification is imperfect, for it neither illustrates fully, for the biochemist, the many structural relationships among antibiotics, nor brings together the biological properties that are of interest to the physician. But it may be the only practicable system in a work which deals, from several points of view, with many substances whose chemical natures are still unknown.

The production, chemistry, antimicrobial activity, and pharmacological properties of individual antibiotics are outlined in a clear and readable manner. Though antibiotics of medical importance have not been given special prominence, the book contains an impressive list of references, extending to the year 1959, for those who wish to explore the medical or other specific aspects of the subject in greater detail.

The authors have produced a useful and extensive work of reference, which is as up to date as can be expected of any work of a comparable type. The book could have been made more nearly comprehensive, however, by the addition of sections on the biosynthesis of antibiotics and on their modes of action.

E. P. ABRAHAM.

THORACIC SURGERY

Surgical Diseases of the Chest. Edited by Brian Blades, M.D. (Pp. 580; illustrated. £8 5s.) St. Louis: C. V. Mosby Company. London: Henry Kimpton. 1961.

In any specialty which is developing rapidly a textbook written on the subject is liable to be out of date by the time it is published. This is certainly possible in the case of thoracic surgery, which now includes so much cardiovascular work within its orbit. However, in this book Professor Brian Blades has collected contributions from a number of acknowledged authorities on different aspects of thoracic disease and produced a concise and well-balanced account of our current knowledge on this subject. Cardiac surgery naturally features prominently, but not to the detriment of surgery of the lungs and mediastinum.

It cannot be expected that individual chapters will not be open to occasional criticism, but, in general, clear writing and good illustrations have given the maximum amount of information in a limited space. The section on the oesophagus by Blades and Hughes is a most concise essay in 30 pages on the surgery of this organ. Many other sections are satisfactory, though one would have liked to see more prominence given to carcinoma of the lung and rather less, say, to mitral insufficiency, which remains one of the real problems of cardiac surgery. De Bakey and Cooley provide a valuable section on the thoracic aorta and the great vessels, and illustrate the scope of treatment that is now offered by prosthetic grafting and bypassing.

The work as a whole is up to date and has no serious omissions. The problem of giving references is solved by giving a few which can be used as a background for more extensive study. The book, dedicated to the memory of Evarts Graham, would, I feel, have full approval from that great surgeon, and it certainly will afford much interest to those who are concerned in thoracic surgery.

T. HOLMES SELLORS.

HOME FOR DIFFICULT CHILDREN

Exceptional Children. Residential Treatment of Emotionally Disturbed Boys at Shotton Hall. By F. G. Lennhoff. (Pp. 201. 21s.) London: George Allen and Unwin Ltd. 1961.

This book describes the residential treatment of emotionally disturbed children and adolescents at the author's school, Shotton Hall, in Shropshire. As Dr. Edward Glover explains in a foreword, the school Mr. Lennhoff has succeeded in building up combines the functions of informal education with those of a psychological first-aid post, a child-guidance unit, a treatment centre, a psychic convalescent home, and a psychological laboratory in which pathological processes can be studied *in vivo*, and the most desirable modes

of normal upbringing inferred and tested. The central aim is to provide a home where children precociously at war with their families can gradually free themselves from those despairing grudges that threaten to embroil them gravely with society. While many of Mr. Lennhoff's policies are based on ideas that have been current in child therapy and in a few of our more enlightened schools for some considerable time, his unique contribution to the techniques of re-education lies in the organization of life at Shotton Hall, whereby the handling of each individual child is regulated by the specific needs and problems of the case, a process which is made to run concurrently with the organization on a similar basis of the needs and problems of the school community as a whole. An approach of this kind must clearly make heavy demands on the staff, and in its staff Shotton Hall has been fortunate, though that is scarcely the appropriate word in view of the painstaking care with which the members are recruited.

It is worthy of note that only about one-third of the cases dealt with are actual or potential delinquents. The others suffer from neurosis or neurotic habits, from regressions of an almost psychotic type, and from various forms of pathological anxiety. All have in common a degree of unhappiness that inevitably leads to maladjustment. This account of the success achieved in dealing with these children makes stimulating reading.

T. FERGUSON.

GUIDE TO THE NEWBORN

The Newborn Child. By David G. Vulliamy, M.D., M.R.C.P., D.C.H. (Pp. 163+vii; illustrated. 15s.) London: J. and A. Churchill Ltd. 1961.

This book has been written as a short guide for doctors who have had comparatively little experience of neonatal paediatrics, and for medical students. What such a reader needs is an account of the routine care of newborn babies, both mature and immature, and an accurate, concise description of the commoner upsets, diseases, and malformations which affect them. There must, of course, be reference to differential diagnosis; and the recommendations about treatment should be as precise as possible. To carry out this assignment successfully requires considerable clinical experience, the ability to see the subject through the eyes of a comparative novice, facility in writing, and sound judgment.

Dr. Vulliamy has accomplished the task very competently and his book deserves a warm reception. Much care has been taken to present the information with a proper sense of proportion, and the advice about treatment is sensible. A few rare conditions are included because they require early treatment, but there is no danger that the reader will be puzzled about what is commonplace and what is unusual. Nor will he make the mistake of undertaking any procedure—for example, subdural exploration—which requires greater experience than he is likely to have. I suggest that in the next edition it would be helpful to give a description of the manual expression of breast milk.

There are 34 good illustrations, and a useful list of suggestions for further reading is included. There are mis-spellings of nasi (p. 15) and of two surnames, Farquhar (p. 152) and Gairdner (p. 153).

NORMAN B. CAPON.

D

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Diabetes in an English Community. A Study of its Incidence and Natural History. By Joan B. Walker, M.D., and David Kerridge, B.Sc. (Pp. 46; illustrated. 7s. 6d.) Leicester: Leicester University Press. 1961.

Hospital Pharmacy Planning. A Guide for Hospital Pharmacists, Architects and Hospital Administrators. (Pp. 48; illustrated. 5s. 6d.) Harrow, Middlesex: Guild of Public Pharmacists. 1961.

The Fixed Eruption. A Possible Hazard of Modern Drug Therapy. By Ashton L. Welsh, M.S., M.D. (Pp. 248+xv. 78s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Psychiatry. Volume I. ***Principles.*** By E. Eduardo Krapf, M.D. (Pp. 224+x; illustrated. $6.50.) New York and London: Grune and Stratton Inc. 1961.

Hypertension. A Mount Sinai Hospital Monograph. Edited by Milton Mendlowitz, M.D. Contributions to the symposium by members of the staff of the Mount Sinai Hospital, New York. (Pp. 156; illustrated. $6.50.) New York and London: Grune and Stratton. 1961.

Biochimie Médicale. Part I. ***Les Constituants de la Matière Vivante.*** By P. Boulanger, J. Polonovski, F. Tayeau, P. Mandel, and G. Biserte. Sixth edition. (Pp. 1-237+x; illustrated. NF. 20.) Paris: Masson et Cie. 1959.

Biochimie Médicale. Part II. ***Enzymes et Métabolismes.*** By P. Boulanger, J. Polonovski, F. Tayeau, P. Mandel, and G. Biserte. Sixth edition. (Pp. 238–519; illustrated. NF. 27.) Paris: Masson and Cie. 1960.

Biochimie Médicale. Part III. ***La Cellule, les Tissus, les Organes, les Humeurs, les Sécrétions.*** By P. Boulanger, J. Polonovski, F. Tayeau, P. Mandel, and G. Biserte. Sixth edition. (Pp. 239–519+xiii; illustrated. NF. 33.) Paris: Masson et Cie. 1961.

Pregnancy and Diabetes Mellitus. By Lars Hagbard, M.D. (Pp. 101+vii. 54s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Stoke Park Studies. Mental Subnormality. Second series. World Mental Health Year Memorial Volume. By J. Jancar, M.B., B.Ch., B.A.O., D.P.M. (Pp. 135+x; illustrated. 30s.) Bristol: John Wright and Sons Ltd. 1961.

Myxedema. By Jerry K. Aikawa, M.D. (Pp. 106+ix. 40s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Hypnotherapy with Children. An Introduction to Child Guidance and Treatment by Hypnosis for Practitioners and Students. By Gordon Ambrose, L.M.S.S.A. (Pp. 160. 12s. 6d.) London: Staples Press. 1961.

Foundations of Psychopathology. By John C. Nemiah, M.D. (Pp. 338+xx. 52s.) New York and London: Oxford University Press. 1961.

The Genesis of the British National Health Service. By John and Sylvia Jewkes. (Pp. 67+xi. 6s. 6d.) Oxford: Basil Blackwell. 1961.

The Health of People Who Work. Edited by Albert Q. Maisel. (Pp. 268+xiii. 40s.) New York: The National Health Council. Oxford, London, Paris, and Frankfurt: Pergamon Press. 1961.

Cross-Cultural Studies in Mental Health. Identity. Mental Health and Value Systems. Edited by Kenneth Soddy. (Pp. 271+xii. 25s.) London: Tavistock Publications. 1961.

Clinical Diagnosis by Laboratory Examinations. By John A. Kolmer, M.S., M.D., Dr.P.H., Sc.D., LL.D., F.A.C.P., F.A.C.D. (Hon.). Third edition. (Pp. 543+xix; illustrated. $10.) New York: Appleton-Century-Crofts, Inc. 1961.

The Stages of Human Development before Birth. An Introduction to Human Embryology. By E. Blechschmidt, M.D. (Pp. 684; illustrated. 96 Swiss Fr.) New York and Basel, Switzerland: S. Karger. 1961.

Let's Eat Right To Keep Fit. By Adelle Davis, A.B., M.S. (Pp. 322+xiii. 21s.) London: George Allen and Unwin Ltd. 1961.

The Year Book of Endocrinology. (1960-1961 Year Book Series.) Edited by Gilbert S. Gordan, M.D., Ph.D., F.A.C.P. (Pp. 408; illustrated. 60s.) Chicago: Year Book Medical Publishers Inc. London: Interscience Publishers Ltd. 1961.

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OXYGEN AND RADIOTHERAPY

Radiobiologists, notably L. H. Gray and his colleagues,[1] have fully established that cells with a normal supply of oxygen are sterilized by about one-third of the *x*-ray dose necessary to produce the same degree of damage if the cells are completely anoxic. Increasing evidence also shows that in nearly all types of neoplasm there are regions, or at least groups of cells, which are practically anoxic.[2 3] These cells may survive the largest dose of *x* rays which can be given in clinical practice, and lead to recurrence of the growth, for very few viable cells may be sufficient to propagate a tumour.[4]

Recent work suggests, more and more, that the reproductive capacity of all mammalian cells may be destroyed by a very similar dose of *x* rays,[5–12] and that the dose required is related only to the number of reproducing cells, their oxygenation, and the number of fractions in which the dose is given.[13 14] If all the cells were well oxygenated, and the dose were to be given in as few fractions as possible, there would not theoretically be much difficulty in sterilizing moderate-sized tumours by modern radiotherapy.

At present the only practical way of increasing the concentration of oxygen around tumour cells is for the patient to breathe oxygen, and it seems likely that in most tumours a sufficient increase in concentration of oxygen will be obtained only if the patient breathes it at high pressure.[15] If an adequate increase in blood flow through a tumour could be obtained oxygen at atmospheric pressure would probably suffice, or it might not be necessary to give oxygen at all. There is, however, no way known yet of increasing the flow of blood through tumours other than by radiotherapy itself.

Changes occur after radiotherapy which result in increased oxygen tensions within tumours.[16] Three interrelated mechanisms probably operate. First, the "tissue pressure" in tumours is increased, and may cause partial obstruction of the venules, leading to slowing of the blood flow.[17] When the tumour shrinks after irradiation the tissue pressure drops and the obstruction of the venules is relieved.[18] Secondly, the demand for oxygen is diminished because of the smaller number of cells surviving in the tumour. Thirdly, inflammation after cell death will improve the blood supply.

In view of all these factors it may well prove advisable to alter the conventional technique of treating tumours with daily doses of *x* rays over a period of four weeks or more, and instead to give a single dose and then wait for a period before giving the remaining dose in the smallest number of fractions over the shortest possible time. The addition of oxygen will be especially important during the first dose, but theoretically an improvement in results should be obtained even if facilities for giving high-pressure oxygen are not available.

Though there is a wealth of data on the effects of oxygen administered during the irradiation of animal tumours,[19–21] to date the preliminary results of only four clinical trials have been published. K. A. Hultborn and A. G. Forssberg[22] treated four patients with skin carcinomas. The tumours were divided into two fields of equal size for irradiation. One field was irradiated while the patient breathed oxygen at atmospheric pressure and the other field was irradiated three to five hours later with the patient breathing air. In all four cases they found that the effect of irradiation was increased by oxygen. Skin tumours were also treated by H. von. Saal and W. A. Dalicho.[23] Because of the poor blood supply of many neoplasms they considered the local administration of oxygen was preferable to inhalation. They therefore injected 20–60 ml. of oxygen into the tumour area so that a cushion of oxygen was formed, or in the case of ulcerated tumours they directed a stream of oxygen under pressure at the surface during the period of irradiation. In 32 tumours thus treated they found that half the *x*-ray dosage was necessary compared with 112 similar tumours irradiated in air. Though their work suggests that an increase in radio-

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[29] Howard-Flanders, P., and Wright, E. A., *Nature (Lond.)*, 1955, **175**, 428.
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sensitivity was obtained, it is difficult to interpret owing to the wide variety of total doses and overall treatment times used and their method of administering oxygen. J. S. Mitchell[24] treated a series of patients with histologically proved carcinoma of the bronchus that had been found inoperable at thoracotomy. Judging the results from those patients who survived more than twelve months after treatment, he found a statistically significant improvement with the use of oxygen at atmospheric pressure. Seven of thirteen patients treated with oxygen survived more than twelve months as compared with only four of thirty-two patients who were treated in air.

The largest clinical trial was initiated by I. Churchill-Davidson and his colleagues in 1954, treating patients breathing oxygen at a pressure of 3–4 atmospheres absolute in a pressure chamber.[25 26] From the first eight patients who were treated evidence obtained from microscopic examination of the irradiated tissues strongly suggested that the addition of oxygen enhanced the radiotherapeutic effect.[27] Subsequently, 108 patients with tumours at many different sites had been treated by the beginning of 1961.[28] The criteria for their selection were: (1) the whole malignant growth, both primary and any secondary deposits, could be included in a radiation field of reasonable size (20 by 20 cm.); and (2) there was considered to be little, if any, chance of cure by conventional radiotherapy. The total number of patients is still small and the time which has elapsed since the treatment of some is short, but in view of the material selected the results are encouraging. Of those who could be assessed 20 (21%) are alive with no evidence of growth for periods up to five years after treatment, and in 41 (42%) there has been apparently complete regression of the primary and secondary growth in the irradiated area. All patients were treated with a much smaller dose fractionation (2–6 fractions) than usual in conventional radiotherapy and over a much shorter period (1–2½ weeks). As would be expected, the smaller and more vascular tumours have shown the greatest "oxygen effect." Particularly interesting features have been the enhanced response of secondary squamous cell carcinoma in lymph glands, which is notoriously resistant to conventional radiotherapy, and the almost complete absence of radiation sickness in spite of the large areas irradiated in some patients and the large doses given in each treatment fraction.

The one serious complication has been an increased incidence of cartilage necrosis. Although in some cases the necrosis has obviously been due to invasion of the cartilage by growth, it is certain that cartilage, which is probably relatively poorly oxygenated, is more liable to damage by *x* rays if the patient is breathing high-pressure oxygen. This was predicted by P. Howard-Flanders and E. A. Wright,[29] who advised making the tumour anoxic and giving three times the normal radiation dose.[30] While it is possible to make a limb anoxic for the period required to give such a dose comparatively few tumours occur in the limbs, and the maximum period for which it is possible to make a whole patient anoxic with safety is under 30 seconds. Even with the most modern and expensive radiotherapy apparatus it is not possible to deliver a dose of the required size in so short a time to deep-seated tumours. It is hoped to avoid the complication by an adjustment of dose level and the use of high-energy irradiation, which is less absorbed in cartilage.

EXPERIMENTAL STUDIES OF CEREBRAL BIRTH INJURY

In recent years more attention has been paid to other than purely traumatic causes of cerebral injury at birth—for example, anoxia. As well as obstetric complications, genetic and biochemical influences can harm the infant, but for the sake of simplicity anoxia and trauma may be considered as the main single agents affecting the brain. Of these two anoxia is the greater danger to the infant at about the time of birth,[1] and it is probably also a common cause of brain injury in newborn babies.[2 3]

The precise mechanism by which anoxia damages nervous tissues is not known, and an elucidation of the biochemical lesions produced may lead to a fresh therapeutic approach to this group of disorders. The brain utilizes glucose almost exclusively for production of energy.[4] Experiments on animals deprived of oxygen have shown that lowering the blood sugar shortens their survival,[5] and in addition that hypoglycaemia alone can produce brain lesions similar to those produced by anoxia.[6] High-energy phosphate compounds are used in the brain to provide energy to maintain the integrity of the cell membrane, and D. B. Tower[7] has shown that in the central nervous system during anoxia the level of creatine phosphate falls and that of organic phosphate rises. However, A. Geiger has presented evidence that such energy can be produced in the absence of carbohydrate substrate,[8] and that electrical activity could be maintained in the absence of glucose if nucleotides were present. In the light of this it is interesting that H. E. Himwich[9] found that nucleotides could protect newly born animals from the effects of anoxia.

A further complication to the biochemical intricacies of brain metabolism is the difference in

response to lack of oxygen of mature and immature animals. J. B. Ranck and W. F. Windle,[10] for example, have produced asphyxial cerebral damage in newborn monkeys which has involved only brain-stem nuclei, sparing the cerebral and cerebellar cortices—which are highly susceptible in the adult. The observation that newborn animals are relatively resistant to anoxia has recently been correlated with their ability to increase rapidly the rate of glycolysis when the oxygen supply is reduced.[11] Survival of the newborn animal in an atmosphere of nitrogen depends on the presence of glycogen in the myocardium,[5 12 13] and when this is depleted the circulation fails. Although in the young animal the heart is more susceptible to lack of oxygen than is the brain,[14] J. C. Mott[12] points out that the brain requires glucose and an efficient circulation, and that these will be lacking if the heart fails. The explanation of such peculiarities of response in the newborn animal is largely speculative. We do not yet understand enough about the maturation of enzyme systems,[15] salt and water metabolism[16 17] in the brain, and the functions of the blood–brain barrier.[18]

In man, epidemiological investigations have shown a positive correlation between intellectual subnormality and cerebral palsy on the one hand and, on the other, obstetric complications,[19] prolonged apnoea at birth,[19] maternal anaesthesia during labour,[20] and other evidence of perinatal anoxia.[21] The association between prematurity and cerebral palsy,[22] when not due to severe jaundice of the newborn, may partly depend on the greater susceptibility of these infants to anoxia,[3] but perhaps we are not yet able to pinpoint a single factor such as this. Necropsy studies[3] have shown that the subarachnoid and intraventricular haemorrhages in the newborn are due to anoxia, while subdural haemorrhages are always traumatic in nature. Chronic brain lesions such as gliosis or cavitation of the centrum semiovale, loss of neurones in the cerebral cortex or basal ganglia, status marmoratus, and ulegyria may also be due to damage at or near birth,[2] but in each individual case it is difficult to assess whether trauma or anoxia is the more important factor or whether other influences are operative. Retrospective epidemiological studies on children with cerebral palsy have indicated that mechanical factors are less important[23] and that the proportion of cases due to trauma is declining as obstetrical practice advances.[24] A question of great clinical importance arising from these studies is whether the magnitude of brain damage is proportional to the degree of anoxia or other stress, or whether a threshold exists the level of which is determined by genetic or environmental factors.

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THE PANCREATITIS PROBLEM

There are two classical theories to explain the aetiology of acute pancreatitis. E. L. Opie's[1] theory of biliary reflux into the pancreatic duct is the one most supported by surgical and post-mortem findings. The case described by Opie which led to the introduction of his theory was an unusual one, for a gallstone had become impacted at the sphincter of Oddi. It is, however, an interesting fact that acute pancreatitis is found almost exclusively in patients with a common termination to the main pancreatic and common bile ducts. Although a gallstone impacted as in Opie's case is unusual, the biliary apparatus commonly is diseased in acute pancreatitis, gallstones being found in the gall-bladder in about 50% of cases.

The second theory, propounded by A. R. Rich and G. L. Duff,[2] is based on the observation that epithelial hyperplasia can be found in the pancreatic ducts in some cases, and it was believed that intrapancreatic obstruction could be produced by this change. This in turn might initiate the chemical changes which lead to the onset of acute pancreatitis. Some observers feel that these histological changes are of little importance in the aetiology of acute pancreatitis, though they may result in fibrosis and atrophy of the gland.

In a recent review D. A. Dreiling[3] discusses some of the other factors which may be significant in the development of acute pancreatitis. Secondary vascular changes may have a role in converting localized inflammatory changes into those of frank tissue necrosis. Spasm of the sphincter of Oddi, though a difficult factor to assess, could be important in the initiation of the acute pancreatitis complicating alcoholism, particularly as alcohol stimulates the gland to secrete. Autoimmune and allergic factors are apt to be invoked as causes of disease when more usual causes are difficult to find, and they have also been put forward as possible causes of acute

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[7] Cope, O., Culver, P. J., Mixter, C. G., Jr., and Nardi, G. L., *Ann. Surg.*, 1957, **145**, 857.
[8] Klatskin, G., and Gordon, M., *Amer. J. Med.*, 1952, **12**, 3.
[9] Albrink, M. J., and Klatskin, G., ibid., 1957, **23**, 26.
[10] Shaper, A. G., *Lancet*, 1960, **1**, 1223.

pancreatitis. It is worth remembering that about 25% of all cases of acute pancreatitis reported in the American literature occur in alcoholics,[4] while such an association is rare in Great Britain,[5 6] partly no doubt because of the lower incidence of alcoholism.

If we have some ideas on the aetiology of acute pancreatitis we are particularly ignorant about the way in which chronic pancreatitis arises. It is not always preceded by an acute attack, and detection is made difficult by the occurrence of "silent" and "painless" cases. Dreiling reports that in only 70% of patients with chronic pancreatitis was there a history of biliary-tract disease or alcoholism, and presumably in Britain an even higher percentage must be of unknown cause. It is therefore important to bear in mind other diseases associated with chronic pancreatitis so that the number of cases of unknown aetiology may be diminished. Hyperparathyroidism[7] may be associated with it, and the pancreatic calcification may be related to the high level of calcium in the blood. Hyperlipaemia, either familial[8] or following acute alcoholic bouts,[9] may likewise be associated with chronic pancreatitis. A form of chronic pancreatitis is also seen in patients with malnutrition, either secondary to alimentary disease or in underfed populations.[10] Calcification may extend throughout the body, and, though it is tempting to attribute this to a progression of the histological changes seen in the pancreas in some forms of protein malnutrition, this is by no means proved. These rarer causes of chronic pancreatitis do not explain more than a small fraction of all cases. An aetiological study of a large series of cases in Great Britain, where alcoholism and malnutrition are rare, would be well worth while.

STRONTIUM-90 IN HUMAN BONE

Although the current rate of deposition of fall-out is lower than at any time since 1954, the heavy discharge of radioactive debris from nuclear weapon tests during 1958 is still a significant factor in the contamination of human bone. The Medical Research Council's latest report[1] shows that levels of strontium-90 in infant bone, which increased sharply in 1959, were maintained with little change in 1960. There is some evidence of a decline in the latter part of the year. This trend would probably have continued if no more hydrogen bombs had been exploded, and there were hopes that the results of the analyses might have become mainly of academic interest—but the hope must now be deferred.

Since strontium has chemical affinities with calcium, and since the radioactive isotope is not a permanent constituent of the environment, the concentration of strontium-90 in new bone gives the most sensitive indication of its passage through food chains and subsequent incorporation in the body. Random sampling is not possible, since the analytical process requires a fairly large specimen—normally a femur obtained at necropsy. The British investigations are largely the work of two teams. Since 1955 the Atomic Energy Authority has completed nearly 800 analyses, using bone samples gathered mainly from the wetter regions of Wales and North-west England. The geographical distribution is important because the amount of fall-out at any place in Britain is roughly proportional to the rainfall. Since the beginning of 1959 more than 200 samples have been collected and analysed by an independent team in Glasgow.

The Atomic Energy Authority's results for the first half of 1960 are now available. In the age group between 2 weeks and 5 years the mean value for the concentration of strontium-90 was 3.3 S.U.—hardly different from the figure of 3.2 S.U. found in the latter half of 1959 (1 strontium unit = 1 $\mu\mu$c of strontium-90 per gramme of calcium). In the same age group the Glasgow results fell from the 1959 level of 2.5 S.U. to 2.3 S.U. in the first half of 1960 and to 1.95 S.U. in the second half of the year. The highest value found in 1960 was 6.6 S.U. for a 4-months-old child from Renfrewshire. These figures may be compared with the Medical Research Council's "warning level" (calculated as the average for any age group) of 33 S.U.[2]

The Atomic Energy Authority has also just issued a report[3] on radiostrontium and radiocaesium in drinking-water in the United Kingdom. The mean strontium-90 content of supplies derived from reservoirs and lakes reached a maximum in the third quarter of 1959 and has decreased since then. The decrease in concentration was faster in rain than in water supplies.

ACUTE DIABETIC ABDOMEN

Patients in diabetic ketosis may occasionally experience severe epigastric pain. As several correspondents have recently pointed out,[4–6] the pain may be sufficiently severe to suggest a perforated peptic ulcer or other surgical condition. To make the diagnosis of diabetes in these circumstances it is necessary to have what the Americans call "a high index of suspicion." A urine test should be considered an integral part of any complete physical examination. Diagnosis and treatment are urgently needed, for the deaths which still occur in diabetic coma are nearly always when there has been some delay in giving insulin.

When abdominal pain occurs in diabetic ketosis it is usually diffuse and unassociated with rigidity. Anorexia is sometimes the first symptom. The patient usually complains of nausea, often vomits, and may be drowsy. Occasionally there is upper abdominal distension due to dilatation of the stomach. Even when glycosuria and ketonuria are present, the diagnosis may remain in doubt, for, as I. T. Lorentz[7] pointed out,

[1] *Assay of Strontium-90 in Human Bone in the United Kingdom: Results for 1960, Part I, With Some Further Results for 1958 and 1959* (Medical Research Council Monitoring Report Series No. 2), 1961. H.M.S.O., London. Price 1s. 3d. net.
[2] *The Hazards to Man of Nuclear and Allied Radiations: A Second Report to the Medical Research Council*, 1960. H.M.S.O., London. See *Brit. med. J.*, 1960, 2, 1947.
[3] Crooks, R. N., Osmond, R. G. D., and Webber, T. J., *Radiostrontium and Radiocaesium in Drinking Water in the United Kingdom—Results to December, 1960*. H.M.S.O., London, 1960. Price 3s. net.
[4] Dipple, P. E., *Brit. med. J.*, 1961, 1, 1108.
[5] Lawrence, R. D., ibid., 1961, 1, 1246.
[6] Chatterjee, A. K., ibid., 1961, 1, 1539.
[7] Lorentz, I. T., ibid., 1961, 1, 1684.
[8] Wyatt, A. P., ibid., 1961, 1, 1685.
[9] Ask-Upmark, E., ibid., 1961, 2, 55.
[10] Pellegrini, R., ibid., 1961, 2, 110.

an acute abdominal emergency in a diabetic may precipitate ketosis and the two conditions may therefore coexist.

Since diabetics are not immune from other illnesses there are a variety of other medical causes of abdominal pain that may also give rise to confusion in the occasional case.[6 8-10] The incidence of atherosclerosis is high among diabetic patients, while myocardial infarction, mesenteric vascular occlusion, and dissecting aneurysm may all present with abdominal pain. The poorly controlled diabetic is also susceptible to infections, and those which may cause severe abdominal pain include gastroenteritis, pyelonephritis, pneumonia with pleurisy, and, in children, pneumococcal or tuberculous peritonitis.

When diabetic ketosis is diagnosed in a patient who has severe pain the possibility of an associated surgical condition should not affect the immediate treatment. First priority must be given to control of the patient's diabetes, for an operation on an uncontrolled diabetic may be fatal. Soluble insulin should be given by the practitioner who first sees the patient, and, if the patient's previous insulin requirements are not known, the initial dose should consist of at least 50 units—100 units if ketosis is severe. After transfer to a hospital casualty department or ward, and after any further treatment with intravenous saline and insulin which may be necessary the patient's blood-sugar level is estimated and the abdominal pain reassessed. Abdominal signs and symptoms that are due to diabetes improve as the ketosis is controlled, and by the time the patient is fit for operation it may become apparent that, after all, surgery is not required.

PERSONAL MEDICAL RECORDS

In a letter published at p. 705 in this issue Drs. John Fry, H. J. Parish, and D. A. Cannon give cogent reasons why agreement should be reached on a scheme for having personal medical records immediately accessible in case of emergency. Many of the examples quoted by Dr. Fry and his colleagues show the difficulties and dangers which can arise if information is not available when it is needed about previous active or passive immunization against tetanus. All are agreed that in certain circumstances it is helpful, and indeed sometimes life-saving, if patients carry about with them in some form or another personal medical details. Many suggestions have been made about how this might be done, but the difficulty is to devise a record which the patient, especially if a child, is likely to have on him when the need arises. Tattooing[1] has obvious possibilities, but would hardly be suitable for recording a series of immunizations; and record cards, even if in a readable state, are apt to be left at home just when they are wanted.[2] A useful scheme is operated in California and in some other parts of North America by the Medic-Alert Foundation, a non-profit-making organization. Patients are provided with bracelets or lockets bearing such items of information as "Allergic to Penicillin," "Hemophilia," "Diabetes," or "I am taking Anticoagulants," and doctors and hospitals can ring up the Foundation for additional information recorded on cards in a central registry. In Britain some local authorities might be able to answer promptly inquiries about a child's immunization history, but a great many others would probably want "notice of the question."

Dr. Fry and his colleagues refer to the record disks described some time ago in this journal by Dr. Parish,[3] but who is going to pay for these disks and how can the public be persuaded that it is to their advantage to carry them? There is an opportunity here for local authorities at least to experiment with some such scheme, which would necessitate the co-operation of local doctors and an educational campaign directed especially to the parents of children receiving a series of immunizing injections. In the meantime much anxiety, and possibly disability, could be avoided if, as Dr. Fry and his colleagues urge, doctors were "scrupulously careful about giving other doctors as much useful information as possible."

1 Lake, N. C., *Brit. med. J.*, 1959, 2, 141.
2 Riddell, J., ibid., 1960, 2, 1239.
3 Parish, H. J., ibid., 1959, 1, 640.

HERPETIC WHITLOW

Infections of the fingers by the virus of herpes simplex are commoner than many realize. Most of the lesions, especially the necrotic ones, appear to be primary infections, but the presence of herpetic antibodies may not ensure immunity to reinfection. Young children are most susceptible to primary infection but usually escape because they are far less exposed than some adults, such as nurses, orderlies, dental surgeons, and doctors. Infection is dependent upon a breach in the skin, most common in the nail folds, and a good example of the condition in a staff nurse was recently described by J. R. Ward and L. Clark.[1] Enhanced virulence of the herpes virus may be the factor accounting for the relative frequency of infections of the hand or arm in nurses attending children with eczema herpeticum, probably the most contagious type of herpes.

The simple herpetic lesion is a clear vesicle on an inflamed base and may be solitary or erupt as a small group. A primary infection often becomes bullous and haemorrhagic, developing into a granulomatous nodule with associated lymphangitis and tender and enlarged regional lymph nodes. While herpetic lesions of the skin are usually merely sore and hyperaesthetic, those affecting the tense tissues of the finger pulp and paraungual folds may be as painful as the more common subdermal pyogenic whitlows. Diagnosis may not be difficult if the early vesicles are observed and found to be bacteriologically sterile. Otherwise the pyogenic infections of bullous impetigo or staphylococcal whitlow are more probable, although the isolation of pathogenic cocci does not exclude a herpetic lesion, secondarily infected. Virological and cytological studies of the early vesicles or bullae and serological tests for the presence of herpetic antibodies at the onset and after three weeks should indicate the viral origin and whether

1 Ward, J. R., and Clark, L., *J. Amer. med. Ass.*, 1961, 176, 226.
2 Brain, R. T., *Brit. med. J.*, 1956, 1, 1061.
3 Stern, H., *et al.*, *Lancet*, 1959, 2, 871.

it is a primary or a re-infection. Cheiropompholyx, pustular psoriasis, and the vesicular or pustular "ide" eruptions may present as sterile lesions, but usually are more widely spread and affect both hands. A digital chancre and the granulomatous lesion of orf are more remote possibilities.

Reports of herpetic lesions in contacts have been occasional since 1898, with an increasing number of nurses acquiring such infection on the fingers, hands, or forearms mostly from nursing children with eczema herpeticum. As these reports were mainly confined to the journals of dermatology and paediatrics they escaped general notice, although R. T. Brain,[2] in 1956, referred in this journal to ten cases, while H. Stern and his colleagues[3] reported 52 three years later. In this larger series the herpes virus was isolated in 13 out of 14 subjects examined. Here the odd feature was the observation that only 51% of the affected nurses had demonstrable herpetic antibodies in their sera, in contrast with the usual figures in adults—between 80 to 90% of adults. In Stern's series the source of the virus infection was attributed to the tracheobronchial secretions, but the virus has often been recovered from the nose and mouth of patients with recurrent herpes, so the risk of infection must be disproportionate to the number of digital lesions so far reported. Whether the incidence of herpetic whitlow is as great as these workers suggest awaits further proof.

Localized reinfections with herpes virus usually resolve in 7 to 14 days, but the primary infections are more severe and take twice as long to clear up. The affected sites should be kept dry and protected from pyogenic infection by painting with a solution of proflavine or with spirit of camphor. Relief may be given when the lesions are moist and painful by immersion in hot saline containing 1/2,000 permanganate of potash.

Sir HENRY HEAD, 1861–1940

Henry Head was born on August 4, 1861, and his centenary was celebrated by a meeting at the London Hospital which was attended by a number of his relatives, amongst them Viscount Head, his nephew, and Mrs. Marsden-Smedley and Dr. Rachel Pinney, his nieces. Professor K. W. Cross spoke of Head's paradoxical reflex, which he discovered while working with Hering at Prague before he entered University College Hospital Medical School. Professor Cross pointed out that Head was in several respects in advance of his time. In his insight into the nature of the reflex he anticipated the modern interpretation of it as a means of restoring the *status quo*; he invented for the purpose of his experiments a cuffed intrabronchial tube; and he noted the effect of cooling on the conduction of a peripheral nerve. Head's paradoxical reflex was a demonstration that sudden inflation of the lungs of a rabbit caused a sharp reflex inspiration. Professor Cross has himself demonstrated a somewhat similar reaction in newborn infants, which may play an important part in its earliest inspirations and its first cry.

Dr. Ronald Henson reviewed Head's studies on sensation. He summarized Head's work and conclusions on the organization of sensation in the peripheral nerve, spinal cord, optic thalamus, and cerebral cortex. He felt that in his observations and conclusions Head had made insufficient allowance for his own temperament and for the effect of the observer's attitude upon the subject being tested. He was also influenced by Hughlings Jackson's evolutionary views applied to the nervous system. Many of the criticisms of Head, particularly of his theory of protopathic and epicritic sensibility, were undoubtedly valid. Nevertheless he made some important discoveries, and the form of sensory disturbance which he termed "protopathic" certainly exists, whatever its explanation may be. The most recent physiological work on the organization of different sensory modalities at the level of the cerebral hemisphere may be found to give some support to Head's differentiation of protopathic and epicritic sensibility at that level.

Dr. Macdonald Critchley discussed Head's contribution to our conceptions of aphasia, pointing out that his interest in the subject sprang from his observations on the sensory functions of the cerebral cortex in patients whose wounds had rendered them aphasic. He could not interpret his observations in terms of orthodox theories of aphasia, but found a more satisfactory dynamic approach in the work of Hughlings Jackson. Head's tests for aphasia were little used to-day, and his own classification, always rather tentative, was not very satisfactory. Nevertheless his contribution to the subject was outstanding. He brought psychology and philosophy to the criticism of the existing orthodox views with their concentration on localization, and put in a new light the problem of the intimate relationship between what he called "symbolic formulation and expression" and the processes of thought.

Sir Russell Brain spoke on "Henry Head: the man and his ideas." Head, who was born in Stoke Newington, came of Quaker stock and was a cousin of Lord Lister. From his schooldays onwards he was interested in science, and his keenness was encouraged by some exceptional teachers. He paid two visits to Germany, one instead of his last summer term at Charterhouse, and the other the two years he spent with Hering at Prague in the middle of his Cambridge career. Sir Russell traced Head's interest in sensation from his early studies on the pain of visceral disease, and pointed out that throughout his professional life he remained a general physician. He was an outstanding teacher with a dramatic style and infectious gusto. His wife, Ruth Mayhew, was perfectly suited to him. She was herself a writer and shared all his enthusiasms. Head the man had wide interests which included literature, art, music, and the theatre. A poet himself, he was the friend and doctor of W. E. Henley, and counted among his friends Siegfried Sassoon, Robert Graves, and Robert Nichols. He enjoyed the companionship of young people, and many still recall him with affection. He bubbled over with ideas, and, if he was sometimes uncritical of them, he made lasting original contributions to neurology, not the least of which was his vitalizing influence.

A COMPREHENSIVE DEPARTMENT OF PSYCHOLOGICAL MEDICINE

THE PROBLEM OF THE IN-PATIENT CASE-LOAD: A 12-MONTHS REVIEW

BY

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During the past decade the psychiatric services in the Manchester region have developed according to a unique pattern (Pool, 1959; Leyberg, 1959; Freeman, 1960; Smith, 1960). This has been largely due to the pioneering work of the Regional Hospital Board in forging ahead with comprehensive psychiatric units in general hospital centres throughout the region, these units being planned to meet, so far as is possible, the total psychiatric needs of the respective catchment areas.

The distinguishing feature of an increasing number of these units is that they are truly comprehensive in so far as there is no selection of admissions, and few, if any, of the latter are subsequently transferred to large psychiatric hospitals. The statistics analysed in this paper are derived from a department which adopts such a policy. It is not a so-called "observation block" for the mere sorting out of acute psychoses. Still less is it a unit restricted to the treatment of conditions showing no material conduct disorder or limited to dealing with cases of apparently early onset and good prognosis. So long as a bed is available all the psychiatric cases requiring admission from a population of some 254,000 are admitted; in practice, this means that virtually all the psychiatric in-patients from the catchment area are in fact treated in this department.

At the suggestion of the Ministry of Health, a number of interested personnel have paid visits to the department during the past year and the advice has frequently been proffered that the work done in a unit of this kind should be reported on, especially at a time when so much rethinking and replanning is taking place in connexion with the psychiatric services generally. At a meeting of the Royal Medico-Psychological Association I read a paper based on an analysis of admissions and discharges over a period of three months (Silverman, 1960). The present communication deals with the extension of some aspects of this analysis to a period of 12 months.

The Department

The department under consideration is in Queen's Park Hospital, this being a large general hospital situated in the Borough of Blackburn. At present there is an official complement of 99 beds and the unit is divided, on the male and female sides respectively, into the following sections:

1. *Emergency Sections.*—These are located on the ground floor. The male and female sections each have a complement of 14 beds.

2. *Ambulant Chronic Sections.*—These are adjacent to the emergency sections on the ground floor and each has a complement of 17 beds.

The day-rooms and dining-rooms on the ground floor are utilized by ambulant patients from both the emergency and the chronic sections. All patients on the ground floor who may have to be confined to bed are transferred to the emergency sections for this purpose.

3. *Acute Sections.*—These are located on the first floor. There are 17 beds in the male section and 20 in the female section. These sections are for patients with relatively well preserved personalities who have no marked conduct disorder. Each section has a separate entrance and dining-room and day-room facilities.

It is a completely "open" unit. In addition to in-patients, "day patients" are treated, and there is an out-patient department in the same building which has been planned and equipped specifically for psychiatric purposes. Also a therapeutic social club and "Alcoholics Anonymous" group meet in an appropriate room in the out-patient department.

Medical and Nursing Personnel

I am on the maximum number of part-time sessions and give an average of eight sessions a week to the Blackburn Group of Hospitals. When the establishment is full there are two whole-time registrars and a general-practitioner clinical assistant who spends two sessions a week doing in-patient work under supervision and helping with electric convulsion therapy. Also two senior hospital medical officers from a large psychiatric hospital give between them a total of not more than three sessions a week devoted to follow-up, supportive, and psychotherapeutic out-patient clinics.

Student nurses are included in the establishment (Table I). These students are "general" nurses in training for their S.R.N., both at Queen's Park Hospital and at the near-by Royal Infirmary, and they spend eight weeks in the department as part of their routine training. A scheme is now being prepared for the recognition of the department for part of a post-registration course in psychiatric nursing to enable those nurses who are so desirous to be placed on the psychiatric part of the Register.

TABLE I.—*Nursing Personnel*

Male Wards	Female Wards
1 Assistant chief male nurse (S.R.N., R.M.N.)	1 Assistant matron (R.M.P.A.)
2 Charge nurses (S.R.N., R.M.N.)	1 Ward sister (S.R.N., R.M.N.)
1 Deputy charge nurse (R.M.P.A.)	2 Ward sisters (R.M.P.A.)
1 Staff nurse (S.R.N.)	1 Part-time staff nurse (R.M.P.A.)
9 Assistant nurses (includes 2 females)	8 Assistant nurses
2 Part-time assistant nurses (females)	5 Part-time assistant nurses
2 Student nurses (males and females)	3 Student nurses

Methods and Analysis of Findings

There follows an analysis of admissions and discharges for the 12 months ending February 28, 1961, this being the first 12 months during which the whole department has been fully open in its present form.

Table II shows the total number of admissions in the various age-groups. The total number of admissions for the 12 months is 488. This gives a crude annual admission rate of 1.92 per 1,000. For each sex the greatest number of admissions falls into the 40–59 age-group, but in the 60+ category the number of females admitted is almost double the number of males.

At first, 76% of admissions were taken into the emergency or chronic sections. This was because the majority of cases admitted were of such a nature that

TABLE II.—*Total Number of Admissions in the Various Age-groups (Subdivided According to Sex)*

Males					Females				
0–19	20–39	40–59	60+	Total	0–19	20–39	40–59	60+	Total
6	86	96	39	227	6	73	106	76	261

close observation was considered necessary during the initial stages of in-patient care.

There were 124 admissions (25.4% of the total) under short legal orders, but 115 (92.7%) of these were subsequently transferred to informal status.

For both the informal admissions and those admitted under legal orders the highest proportion of patients fell into the 40–59 age-group. This was followed in each case by the 20–39 age-group. Again in each case the 60+ group came next and the smallest proportion of patients was found in the 0–19 age-group. In other words, the proportion of admissions, informal and under legal orders respectively, according to age-groups, appeared to show a broadly similar distribution.

Of those admitted informally to the emergency wards, 161 (65.2%) were subsequently transferred to the acute section.

Only 35 of the patients admitted to the emergency wards under short legal orders were ultimately transferred to the acute section. This is no more than 28.2% of the total admissions under legal orders. In other words, although 92.7% of the cases admitted under legal orders had improved to such a degree that they could be kept in hospital informally, 71.8% of them were not regarded as suitable for the acute section in which the better-preserved type of patient is accommodated.

Table III shows that the total number of discharges out of the department (including deaths) in the 12 months was 479. As would be expected from the close

TABLE III.—*Total Number of Discharges (Including Deaths and Transfers Out of Department) in the Various Age-groups (Subdivided According to Sex)*

Males					Females				
0–19	20–39	40–59	60+	Total	0–19	20–39	40–59	60+	Total
6	83	87	35	211	7	70	113	78	268

approximation of this figure to the total number of admissions, the distribution of the discharged patients among the respective age-groups (in each sex) was similar to that found among the admissions.

Nine patients (two males and seven females) were transferred to other psychiatric beds. These figures do not include a subnormal male patient who was transferred to a hospital for subnormality or a male patient who was transferred to an epileptic colony.

Although the median length of stay for the male emergency–chronic sections was approximately six weeks, that for the female emergency–chronic sections was four to five months (Table IV). For the whole department the median length of stay was approximately

TABLE IV.—*Median Length of Stay (in Days) for Patients Discharged (Including Deaths) from the Respective Sections of the Department*

	Acute Section	Emergency–Chronic Sections
Males	36·84	44·42
Females	41·42	135·38

two months. In the male wards the shortest stay was one day and the longest 261 days. In the female wards the shortest stay was 1 day and the longest 7,317 days.

Discussion

It has been shown that the crude annual admission rate for this department for the 12 months ending February 28, 1961, was 1.92 per 1,000. The effect of the Worthing experiment (Carse *et al.*, 1958; Carse, 1959) was to reduce the admission rate from 4.11 per 1,000 in 1956 to 1.68 per 1,000 in 1957. As has been pointed out by Parnell and Skottowe (1958, 1959), the crude annual admission rate in Worthing in 1956 was almost two and a half times the national average. Leyberg (1959), in the Bolton area, found that his admission rate was 1.5 per 1,000, this being below the national average of 1.9 per 1,000 given by him for 1958. This latter figure, however, was based on the total number of psychiatric admissions given in the Annual Report of the Board of Control and therefore refers to admissions to designated mental hospitals only. (These admissions would, in fact, work out to a rate per 1,000 of population of 1.9 for 1957, not 1958—Table V.) A more informative annual admission rate for the years prior to the full implementation of the Mental Health Act can only be calculated by taking into account not only admissions to designated psychiatric beds but admissions to undesignated beds in general hospitals, licensed houses, and private single care.

I am indebted to Miss Allbeson, administrative assistant in mental health, Manchester Regional Hospital Board, for supplying figures which take account of these admissions (Table V).

TABLE V.—*Psychiatric Admission Rate (England and Wales) per Thousand of Population*

Year	Home Population, England and Wales	Admissions to Designated Hospitals	Rate per Thousand Population	Total Admissions, All Institutions and Private Single Care	Rate per Thousand Population
1957	44,907,000	88,943	1·9	93,306	2·0
1958	45,109,000	91,558	2·0	95,968	2·12
1959	45,386,000	95,344	2·1	98,237	2·16

It will be seen that the rate per 1,000 for this department (1.92) for the 12 months under review approximates closely to the national average for 1957 (2.0) and is below that for 1959 (2.16), the latter being the most recent national figure available for comparison.

Of the females admitted, 76 (29.1%) were 60 years or more, whereas only 39 male admissions (17.2%) fell into this age-group. Norton (1961) found that 25.7% of all female admissions to a large psychiatric hospital in 1957 were aged 65 or over. Norton also found that the bulk of his female admissions in 1957 were in the fourth, fifth, and sixth decades of life. Though these findings would fit in with my own figure for females, it will be seen that, so far as males were concerned, the majority of admissions were to be found in the second, third, fourth, and fifth decades.

It has been shown that the bulk of the cases admitted were of the kind requiring close observation in the first instance and that 25.4% of the cases admitted were taken in under short legal orders. Macmillan (1956) found that of 542 admissions to a large psychiatric hospital via the "mental health department" in 1955, 262 (48.3%) were admitted under short legal orders. However, for the same year, out of 1,370 admissions

via the out-patient clinic, only 79 were admitted under short legal orders, and one patient (a Broadmoor case) was certified.

In this department 92.7% of those cases admitted under legal orders were subsequently transferred to informal status. Nine cases remained which were not dealt with in this way. Of these, one was a female epileptic with disturbed behaviour who had been admitted from a near-by epileptic colony because of an exacerbation of her disturbed conduct. Her home was in Manchester (a distance of 25 miles from the department), and she was therefore transferred under legal order to a large psychiatric hospital nearer her home. The family of a female paraphrenic, in whom the prognosis appeared to be poor, wished her to be cared for in a private hospital and she was transferred under a legal order to a private psychiatric hospital in South Manchester. A chronic schizophrenic female patient who had been resident in a large psychiatric hospital for many years managed to make her way to Blackburn and was admitted to the department under a legal order. She was transferred back to the large hospital under an order. A subnormal male patient who had aggressive outbursts was transferred under an order to a hospital for subnormality. The other five cases were male patients who were discharged from the department on or before the expiration of their short legal orders.

Although 92.7% of cases admitted under legal orders improved sufficiently to be transferred to informal status, 71.8% of cases admitted under legal orders were not regarded as suitable for the wards in which the better-preserved type of case was accommodated. This finding fits in with the fact that the bulk of admissions were of the kind requiring close observation during the initial stages of in-patient care (76%).

Table III shows that the total number of patients discharged (479) approximated closely to the total number admitted (488). It was considered worth while to examine what effect this admission and discharge rate was having on the resident chronic population, a chronic patient being defined as one who had been an in-patient for two years or more. Table VI shows that the male chronic population was reduced by one and the female chronic population by six. The number of discharges, transfers, and deaths contributing to these figures are given in Table VI, in addition to the destination of the transferred patients.

TABLE VI.—*Changes in Chronic* Population (Including Destination of Transferred Chronic Patients)*

Sex	No. of Chronic Patients on March 1, 1960	No. of Chronic Patients on February 28, 1961	No. of discharges, transfers, or deaths (Chronic Patients) in the 12 months
M	10	9	1 death
F	21	15	1 death ; 2 transfers to geriatric department ; 1 transfer to Part III Accommodation ; 1 transfer to large psychiatric hospital ; 1 subnormal patient discharged home

*A chronic patient is defined as one who has been continuously under care for not less than two years.

There is little doubt that the reduction in the chronic population results, at least to some extent, from a reduced intake of potentially chronic patients. This is made possible very largely by domiciliary visiting by the psychiatrist, the institution of treatment at a relatively early stage, "day-patient" facilities, and the utilization of the services of mental welfare officers, district nurses, home helps, and other ancillary personnel. The mental welfare officer is usually the key worker who, among other duties, acts as a liaison officer between the various personnel and thereby determines the ultimate success of the whole service. Weekly case conferences are therefore held with all the mental welfare officers in the catchment area, and these officers also attend, in rota, at routine ward rounds, out-patient clinics, the therapeutic social club, and domiciliary visits. Such a scheme depends in no small measure on the fact that the hospital psychiatric unit is situated at the very centre of the urban area which it serves. It is part of a local hospital with which the surrounding population is familiar and which is easy of access for both patients and relatives.

Although the median length of stay for patients discharged (including deaths) from the male and female acute sections was approximately five and six weeks respectively, that for the female emergency–chronic sections was three times the median length of stay for the equivalent male wards (Table IV). This larger figure for the relevant female sections was undoubtedly influenced by the greater number of chronic patients dealt with on the female wards (Table VI).

A careful search was made to trace patients admitted direct from the catchment area to other beds in large psychiatric hospitals. During the 12 months the total number was 26, or 5.1% of all cases admitted from the area to psychiatric beds. In other words, the department under consideration was coping with virtually 95% of the total in-patient case-load. In spite of this, the pressure on female emergency beds in particular was often excessively heavy and patients had not uncommonly to be moved out of these beds in order to make way for even more urgent cases. For this reason it has already been agreed to increase the female emergency accommodation by some six to eight beds. Also, it is certainly arguable whether or not some of the aged patients cared for on a "day" basis should not have been dealt with in appropriate local authority hostel accommodation if only such facilities had been available. In many such cases the "day" approach was perhaps only a kind of "stop-gap" arrangement for tackling the problem until adequate hostel facilities are built up.

This department of approximately 100 beds is already coping with 95% of the total psychiatric in-patient case-load from a population of 254,000. This bed complement is a good deal less than has been suggested by those who have attempted to estimate the relevant requirements. Hoenig and Crotty (1959), for example, tried to assess the number of psychiatric beds required to cope with a catchment area involving a population of some 300,000. They concluded that a unit of 200 beds could cope with 93% of admissions, but this conclusion was based on an admission rate of 937 per annum. The latter figure is, in my view, far too high, and Hoenig (in a personal communication) agrees with this criticism.

Tooth and Brooke (1961), basing their estimates mainly on the 1956 admissions for England and Wales, consider that 1,800 psychiatric beds per million of population are required "for all types of care." This, of course, would work out to some 450 beds for a population of 250,000—four and a half times the number of beds in this department. Further on in their

paper, however, Tooth and Brooke state: "Admissions have been steadily rising, but a preliminary count of the admissions in the first six months of 1960, compared with the first half of 1959, shows that while in some hospitals the upward trend has continued there is a substantial number in which there has been a marked decrease. This result may be attributed to an increase in the number of patients treated in out-patient clinics and in day hospitals, and to pre-admission screening." It is presumably due to the latter—and allied procedures—that it has been found that the psychiatric unit need not be as large as recent estimates have suggested.

It is undoubtedly essential to have an active and co-operative geriatric department in the group and the fact that the psychiatric department is an integral part of the general hospital group conduces towards the establishment of the correct relationship. With this important proviso, it is considered that 150 beds are the maximum number required for a well-organized psychiatric department catering for a population of, say, 250,000, and, basing their conclusions on experience gained from the kind of department here discussed, Marshall and Smith (1961) recommend "about 120 beds" for catchment areas of this size within the Manchester region.

Summary and Conclusions

A comprehensive psychiatric department in a general hospital setting has been described. The layout of the department is outlined and the medical and nursing personnel are briefly reviewed. An analysis is made of admissions and discharges for the 12 months ending February 28, 1961. The significance of the findings is discussed.

The crude annual admission rate worked out to 1.92 per 1,000. The number of females admitted in the 60+ age-group was almost double the number of males.

In the first instance, 76% of admissions were taken into the emergency or chronic sections.

Of the total admissions, 25.4% were taken in under short legal orders, but 92.7% of these cases were subsequently transferred to informal status.

The proportion of admissions, informal and under short legal orders respectively, was highest in the 40–59 age-group, followed by the 20–39 age-group, the 60+ age-group, and the 0–19 age-group.

The total number of patients discharged (479, including transfers and deaths) approximated closely to the total number of admissions (488). The male chronic population was reduced by one and the female by six.

The median length of stay for the whole department was approximately two months. The median length of stay for patients discharged from the female emergency–chronic sections was three times that for the equivalent male wards.

Of the total psychiatric admissions from the catchment areas, 5.1% were admitted direct to other beds in large psychiatric hospitals. In other words, the department was coping with virtually 95% of the in-patient case-load. Pressure on the female emergency beds was from time to time excessively heavy.

It is thought that the success of the department was determined in no small measure by domiciliary visiting and the institution of early treatment, day-patient facilities, and the utilization of the services of mental welfare officers, district nurses, home helps, and other ancillary personnel. The mental welfare officer was regarded as the key worker. The whole scheme was facilitated by the location of the hospital department in the very centre of the urban area served.

It was found essential to have an active and co-operative geriatric department within the hospital group. With this proviso, it was concluded that 150 beds were the maximum number required for a well-organized psychiatric department catering for a population of 250,000.

I thank the administrative officers, nursing staff, and mental welfare officers who have co-operated in collecting the relevant statistics.

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BIOCHEMISTRY IN RUSSIA

IMPRESSIONS GAINED AT THE FIFTH INTERNATIONAL CONGRESS OF BIOCHEMISTRY IN MOSCOW

By A Special Correspondent

The Fifth International Congress of Biochemistry, held in Moscow from August 10 to 16, was unique in several ways. Not only was it the first International Congress of Biochemistry to be held in a Communist country, but it was the largest scientific congress ever held in the U.S.S.R. The secretary-general, Academician N. M. Sissakian, estimated that about 6,000 people took part in the various sessions. Among these were 3,500 foreigners from 58 different countries, about 450 coming from Great Britain. Nearly 2,000 contributions were presented.

The congress, which took place under the presidency of Academician A. I. Oparin, was held in the imposing building of Moscow University situated on the Lenin Hills overlooking the town. Symposia were held on the following subjects under various presidents:

1. Biological Structure and Function at the Molecular Level (M. F. Perutz, Cambridge); 2. Functional Biochemistry of Cell Structures (O. Lindberg, Stockholm); 3. Evolutionary Biochemistry (S. Ochoa, New York); 4. Molecular Basis of Enzyme Action and Inhibition (P. A. E. Desnuelle, Marseilles); 5. Intracellular Respiration: Phosphorylating and Non-Phosphorylating Oxidation Reactions (E. C. Slater, Amsterdam); 6. Mechanism of Photosynthesis (H. Tamiya, Japan); 7. Biosynthesis of Lipids (G. Popjak, London); 8. Biochemical Principles of the Food Industry (E. Pijanowski, Warsaw).

Two plenary lectures were given at the beginning and end of the congress, one by D. E. Green (U.S.A.) on "Subcellular Structure and Enzymatic Functions," and the other by F. Sorm (Czechoslovakia) on "Micro-

structure of Protein in Connexion with its Biological Function." Short papers were presented in 28 different sections.

In order to complete such a large programme it was necessary to hold 17 to 18 sessions simultaneously on each of the four working days of the congress. At all the symposium sessions excellent arrangements were made for simultaneous translations, while at the other sessions an interpreter was at hand. The Russian participants understood written English and very many spoke excellent English, so that the language difficulties were probably less than at former congresses. Abstracts of the short communications were published in a separate book. All abstracts submitted in Russian were published together with an English translation. Preprints of the symposium contributions were available in English and Russian. The publishing house of the U.S.S.R. Academy of Sciences was the official publisher of the Russian version, and Pergamon Press Ltd. published the foreign version. The proceedings will subsequently be published in a series of 10 volumes.

Making New Friends

Many of us had seen comparatively few of our Russian colleagues before, and this congress, like other international meetings, provided a wonderful opportunity to meet those we had only previously known by name. Naturally many of the senior Russian biochemists were involved in the organization of the congress and so had little opportunity to show their laboratories to visitors, but many of us gladly took the opportunities that did arise to visit laboratories. In addition, our hosts were most generous with their receptions, and for our part we are most grateful to our ambassador for holding a delightful reception at the embassy which enabled the participants from this country to entertain those who had worked so hard for the success of the congress.

Other occasions for making new friends were on the excellent tours arranged by Intourist: these were conducted by charming guides, who spoke excellent English. In addition, there was an active Ladies' Committee, which was very ready to make arrangements for tours of all kinds.

Scientific Sessions and Exhibitions

So much for the facts of the congress: what of one's impressions? The formal sessions were in general successful in that they achieved what they set out to do. The symposia were aimed to give a broad picture of the subject matter and succeeded in doing this. The short papers, which were designed to give everyone the opportunity of describing his results in a strictly limited time (10 minutes), were well presented. The general feeling was that there were too many simultaneous sessions, so that the size of the audience at any one was sometimes very small.

The exhibitions of books and apparatus were deemed a great success, and it is good to report that Great Britain was well represented in both.

Biochemistry in the U.S.S.R.

It is difficult to write of one's impression of Russian biochemistry, for the time was very limited. While undoubtedly there is much competent work being done in biochemistry, the impression is gained that the subject has been relatively neglected compared with physics and engineering. This was freely admitted by the Russian biochemists with whom one spoke. There is the feeling, however, that having done so well in the physical field more emphasis will now be given to the biological sciences. Practical evidence of this that may be cited was the obvious importance attached to the congress by the Government. Visitors to laboratories saw the new Russian equipment that was just becoming generally available. For example, they now have their own analytical ultracentrifuges and recording spectrophotometers. Further evidence is the formation of the Soviet Biochemical Society, which now has some 2,000 members.

Discussions with individual biochemists showed that they were well acquainted with the advances in the subject taking place in the West. In every laboratory visited there were copies of the more important journals published in English.

Biochemical research is carried on in Moscow in a large number of different laboratories. Not surprisingly the standard of equipment and the work done varies greatly. So far as research problems are concerned, there was much speculation on the likely effect of the rise to power again of Academician T. Lysenko. This event could seriously affect the development of Soviet biochemistry in the aspects of the subject which touch on the chemical basis of heredity. It is progress in this field that has done so much to create the enthusiasm now prevalent among biochemists.

Teaching Problems

The opportunity also arose to discuss the teaching of biochemistry to medical students. This is carried out in Moscow in two separate medical institutes. The one visited had an intake of 1,000 students per year. The biochemistry course is confined to the second year after entry to university. The year is divided into two semesters. During the first semester the students receive two hours of lectures per week and in the second semester three hours. In addition, they attend a practical course lasting three hours each week. The textbook of biochemistry appeared to be of about the same standard as is used in Britain. The main problem is one of numbers, for the present lecture theatre only has space for 250 students, so that the lectures have to be repeated. It is planned to relieve this situation with the construction of a larger theatre. The practicals presented even greater difficulties, since the laboratories are small, and there appeared to be no immediate plans to relieve the situation.

The problems for Soviet biochemistry are not basically different from those in other countries, apart from the possible influence of ideological theories. The major problems for the progress of the subject would seem to be the provision of adequate laboratories, both in terms of apparatus and general facilities, the reduction of the teaching load, where appropriate, and the further encouragement of free discussion and criticism of the results and conclusions of research work. One of the major problems that appear not yet to have been solved is how to provide proper opportunities to the younger scientists. This is a problem in any country, but one gained the impression that in Russia it was further from solution than in Britain, and in comparison with the U.S.A. the difference was even more marked.

Other Impressions

Since the congress was being held in a country in which the political and economic system differed

markedly from that to which most of the participants were accustomed, it was natural that discussions were not confined to purely biochemical topics. The discussion was naturally heightened even more by the timing of the congress, for it was held during the celebrations to mark the successful space flight of Major Titov.

One of the major achievements of the congress was the way it demonstrated how people used to living under different conditions could work together for a common objective. Ill-feelings caused by petty national considerations were virtually unknown. Much of the credit for this is due to the character of the Russian people themselves. Universally their charm, friendliness, and understandable pride in the achievements of their country were admired. While they freely discussed the ways in which their system of government could be improved, one met no one who wished to change the basic concepts. For this reason it is a pity that their scientists are not more free to travel abroad, for nothing could do more for the advance of biochemistry in Russia than the development of a really free exchange between the scientists of East and West. Not only is this important merely for biochemistry. As Sir Rudolph Peters, the president of the International Council of Scientific Unions, pointed out at the closing session, science and scientists can show the way to a closer understanding among the people of the world, and this congress was a magnificent demonstration of this philosophy. We look forward to the next congress in New York in 1964.

New Appliances

PORTABLE ANAESTHETIC APPARATUS WITH VAPORIZER OF NEW DESIGN

Group-Captain R. L. SOPER, principal specialist in anaesthetics, Royal Air Force, writes: In certain localities, on active service, on board ship, etc., and perhaps in time of emergency, there will long be a requirement for an anaesthetic apparatus which is independent of cylinders of gas for its operation. Twelve years ago I described a simple apparatus for administering gas and oxygen to which ether and trichlorethylene vapours could be added (Soper, 1949). By means of an air-inlet valve the apparatus could be used without any compressed gases to vaporize the drugs. It has been felt for some time that improvement could be made on the original design both by replacing the breathing-bag by a bellows to act as a *vis a tergo* as suggested by Stout (1954), and by an improved vaporizer that would be capable of a higher maximum concentration of the volatile anaesthetic agent and a greater constancy of output. By these means its usefulness without gas-flows would be greatly increased.

The result of experiment on these lines has been the production of an entirely new design. The apparatus now consists of a vaporizer, bellows, air-inlet valve, and the associated breathing-tube, expiratory valve, etc. (Fig. 1). Flowmeters can easily be added, and provision is made for mounting them on the base-plate. The main feature of the new model is the vaporizer, which is of original design and has been tentatively called an "ambient temperature vaporizer." That is, for a given atmospheric temperature it provides a reasonably constant output.

While every credit is due to Macintosh and his co-workers for their outstanding work on the development of vaporizers of constant and calibrated output (Macintosh and Mendelssohn, 1941; Epstein and Macintosh, 1956), it is felt that something less exact but simpler in construction and less bulky will be acceptable and fill a need.

The object underlying the design of the vaporizer is to keep the volatile drug at as near to room temperature as possible, and to maintain it at an approximation of that temperature throughout the period of use, thus ensuring a constant concentration of inhaled vapour for a given setting of the control. This has been achieved largely by making the body of the vaporizing chamber of an aluminium alloy

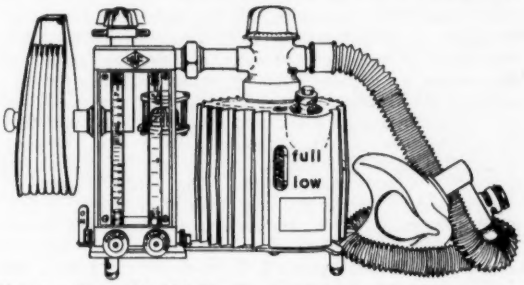
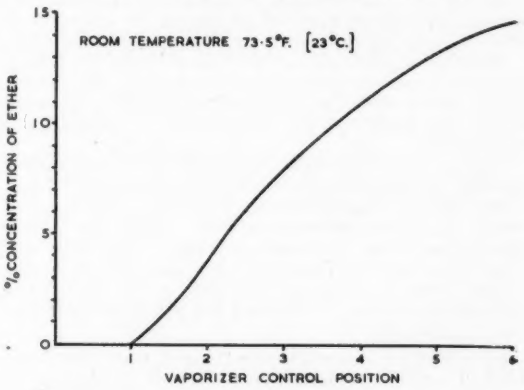
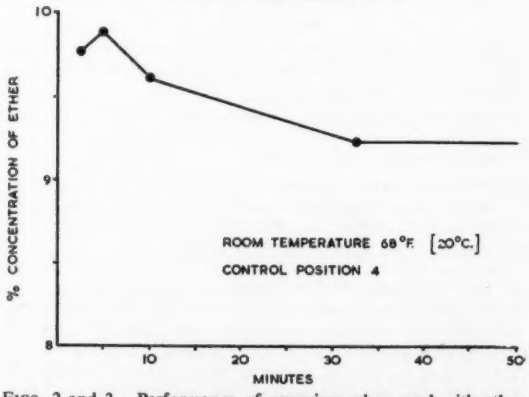


FIG. 1.—Apparatus with flowmeters attached. The air-inlet valve can be seen behind the right-hand flowmeter.





FIGS. 2 and 3.—Performance of vaporizer when used with ether under conditions simulating average respiration on a prototype with less surface area than the production model.

of good heat-conducting properties, placing fins on the outer and inner surfaces to increase the surface area, and leaving the exterior finish a rough casting and colouring it black.

The vaporizing chamber has vertical external fins cast integrally with the body, and horizontal internal fins made separately but a shrunk-tight fit to ensure perfect conductivity of heat. The neck has a similar thread to the glass portion of the standard Boyle's bottle and the M. & I. E. vaporizer with which it is interchangeable. A contents gauge is fitted, so designed that so long as the fluid level remains between two marks the concentration is not materially affected by the actual level. The internal opening

of the filler is below the level of the contained fluid; thus it is possible to "top up" when the vaporizer is in use. The filler is closed with a screw-cap containing a spring-loaded safety-valve. The wick and control assembly of the Thornton vaporizer, as used in my original apparatus, have been retained, but a better scale has been fitted below the control knob.

In use, the vaporizer is most effective. In no case has it been impossible to obtain satisfactory operating conditions for major abdominal surgery using ether–air and no other drug (Figs. 2 and 3), save only a "sleeping dose" of thiopentone to render induction more pleasant for the patient, and, of course, premedication with atropine. When used with ether, during the first 10 minutes of operation the temperature of the vaporizer falls a few degrees; thereafter it remains constant. A corresponding initial fall of vapour concentration occurs. The vaporizer can, of course, be used with drugs other than ether, but it is with this that the constant temperature feature is most noticeable.

When used with a flow of gas and oxygen, the bellows become a breathing-bag: the bellows control should be positioned to place it fully in circuit. When used as a draw-over apparatus, the bellows are normally placed out of circuit, but if some degree of rebreathing is temporarily required this can be obtained by placing the control in a position which allows a slight flow into the bellows.

For artificial respiration the bellows give effective ventilation and can be worked readily with one hand. The tension on the spring of the expiratory valve should be increased during this manœuvre or, alternatively, a Ruben's valve may be used.

The apparatus can easily be carried in one hand while the mask is attached to the patient, it weighs 16 lb. (7.3 kg.).

My thanks are due to Mr. C. W. Palmer, chief technical officer, No. 248 Maintenance Unit, Royal Air Force, Chessington, Surrey, for much assistance in the design and manufacture of the prototype which was shown at the British Medical Association Exhibition in 1957. The apparatus is produced by Medical and Industrial Equipment Ltd., London W.1.

I am indebted to the Director-General, Royal Air Force Medical Branch, for permission to publish this description.

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three times the total concentration in the plasma is required to get the same therapeutic level as can be obtained with sulphadiazine, and these necessary higher concentrations may increase the likelihood of toxicity.

Therapy.—These drugs have been extensively advocated for the treatment of skin infections, though their use in staphylococcal infections is seldom justified. Their virtue lies in the convenience of administration once daily, 0.5 g. or 1.0 g. daily in a single dose being sufficient. Their chief field of usefulness is probably in the management and prophylaxis of *Escherichia coli* infections of the urinary tract. Unfortunately the organisms which are difficult to eradicate from the urinary tract are usually resistant to all sulphonamides, irrespective of their duration of action. For most other infections sulphonamides are not indicated, and excessive use of long-acting sulphonamides may delay the use of effective chemotherapy with more appropriate agents.

Toxic Effects.—The long-acting compounds are liable to cause the same toxic effects, rashes, drug fever, blood dyscrasias, etc., as the short-acting compounds. The persistence of appreciable blood levels for prolonged periods after a single dose is a serious disadvantage if sensitization reactions develop.

N.H.S. Basic Price.—100 0.5-g. tabs.: lederkyn and midicel, 58s. 8d.; orisulf, 17s. 4d., madribon, 37s. 10d.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

LONG-ACTING SULPHONAMIDES

Sulphamethoxypyridazine
("lederkyn," Lederle; "midicel," Parke, Davis, who also market the N¹-acetyl derivative in a suspension).

Sulphaphenazole
("orisulf," Ciba).

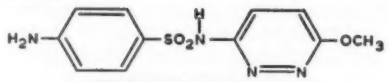
Sulphadimethoxine
("madribon," Roche).

Chemistry:

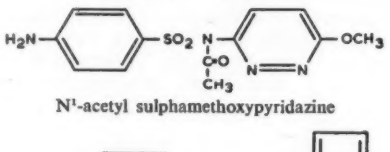
Sulphamethoxypyridazine is 3-*p*-aminobenzenesulphonamido-6-methoxypyridazine.

Sulphaphenazole is 1-phenyl-5-sulphanilamidopyrazole.

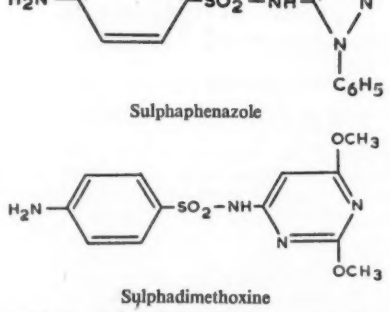
Sulphadimethoxine is 2,4-dimethoxy 6-sulphanilamido-1,3-diazine.



Sulphamethoxypyridazine



N¹-acetyl sulphamethoxypyridazine



Sulphaphenazole

Sulphadimethoxine

Pharmacology.—The action of these compounds is similar to that of other sulphonamides and is primarily bacteriostatic. They interfere with the utilization of *para*-amino benzoic acid by infecting organisms. They are definitely not bactericidal, and their bacteriostatic effect is reduced in the presence of pus.

All these compounds are slowly excreted, and this leads to prolongation of the period during which high blood levels of sulphonamide may be recorded. On the other hand, these compounds are much more extensively bound to plasma protein than is, for example, sulphadimidine, and this consequently results in lower diffusible concentrations in the plasma. It is the diffusible concentration which determines their antibacterial effect, as protein-bound sulphonamide has no activity. Sulphamethoxypyridazine and sulphaphenazole are acetylated in the liver, and sulphadimethoxine is excreted in the form of a very soluble glycuronide.

Because of the degree of protein binding, very much higher total concentrations of these compounds in the plasma are necessary to achieve the same diffusible, and therefore therapeutically active, concentration as can be achieved with lower total concentrations of sulphadimidine. In the case of sulphamethoxypyridazine and sulphaphenazole about

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Personal Medical Records

SIR,—A scheme for personal records that are immediately accessible, and readily decipherable, in an emergency should come into widespread use without further delay. Liaison between doctors in different medical fields should be improved, and facts that may have an important bearing on a patient's medical treatment should be passed on by records and other means. Essential records should be carried on the person at all convenient times for reasons such as the following:

(1) A child has received all injections, primary and reinforcing, of tetanus toxoid at the correct intervals. In the absence of records he is subjected on injury to the serious hazard and discomfort of tetanus antitoxin (which he does not require).

A variation of the same difficulty arises when a mixed vaccine is alleged to have been given, but it is not known whether it included tetanus toxoid. Only an exact record will supply the evidence.

(2) An ex-Service man has accepted all his anti-tetanus inoculations while in the Forces. Unless he can produce details quickly in an emergency after he returns to civil life, he incurs a similar risk of being given serum unnecessarily.

(3) A question that should be asked before tetanus antitoxin or other serum is administered is, "Have you ever had serum before?" The patient knows he has received many injections, but he is usually quite uncertain of their nature, and tends to confuse sera, vaccines, and even antibiotics. Both patient and doctor are consequently at a grave disadvantage.

(4) An anti-tetanus injection given by a casualty officer is assumed to have been antitoxin, whereas it was a first dose of toxoid; when the patient develops tetanus (from which he subsequently dies), the spasms are at first provisionally diagnosed by a puzzled doctor as due to meningitis. The diagnosis is corrected only after admission to another hospital.

(5) A boy of 18 years, who has received periodic reinforcing doses of tetanus toxoid at school, is injured on the rugby field. Unless information can be produced from his wallet in the dressing-room that the last injection of toxoid was within five years antitoxin will be given, and rightly so. In the absence of an authentic record, he must be regarded as non-immune (or incompletely immunized). And he could be an asthmatic—another fact which should be known to any doctor called to attend him.

(6) A patient with an urticarial rash presents himself at the family doctor's surgery. An injection of tetanus antitoxin had been given ten days previously at a hospital many miles away. No record is available, and only an experienced doctor might establish a connexion between the rash and serum.

(7) A woman shows her doctor a scar on her arm and tells him that it is the result of smallpox vaccination, whereas it was due to B.C.G. In the belief that she was protected, she could have been exposed to the risk of smallpox.

(8) Details of the following may be of supreme value in certain emergencies: blood groups, idiosyncrasies, sensitivities (serum, bee-sting, drugs, etc.), current medications, and certain diseases (haemophilia, diabetes, epilepsy, myasthenia gravis, etc.).

What should be done? Doctors should be scrupulously careful about giving other doctors as much useful information as possible. Hospitals should always inform the family doctor about injections of tetanus antitoxin and toxoid. A suitable space for such essential personal details should be made available on the patients' medical record envelopes which the family doctor possesses. Patients should be made to realize that it is to their advantage to have and to produce essential information. Personal record cards or disks should be carried, whenever practicable, on the person: disks may be worn as lockets or bracelets, or even carried loose in the pocket.[1] When there is an accident or other emergency doctors should ask for the authentic records of previous immunizations before they give injections that may be both dangerous and unnecessary.

We have reason to believe that errors in procedure are made every day, and we appeal to individual doctors to play what part they can, even in the absence of central direction and a standardized record card.—We are, etc.,

JOHN FRY,
General practitioner.
H. J. PARISH,
D. A. CANNON,
Wellcome Research Laboratories.
Beckenham, Kent.

REFERENCE

[1] *Proceedings of a Symposium on Immunization in Childhood*, 1960, E. and S. Livingstone, Edinburgh and London.

Electric Convulsion Therapy

SIR,—Thanks to the pioneering work of Dr. Louis Rose and his colleagues suxamethonium is now widely used as a muscle relaxant in electroconvulsion therapy. I am, however, a little perturbed about Dr. Rose's advice (August 26, p. 582) that it is better to give "more than less" of suxamethonium: "A little more can do no more harm (prolonged apnoea is rare—I have never met it in something like 2,000 patients). . . ."

One in 2,000 is just about the frequency observed of homozygotes for the abnormal pseudocholinesterase gene who are liable to produce a prolonged apnoea. This may not seem much to any one individual practitioner, but forms a considerable number of incidents if all those treated with electroconvulsion are taken into account. It is best as a matter of principle to limit the dose of suxamethonium chloride to 30 mg. for new patients. This will not prevent a prolonged apnoea, but will restrict it to the less dangerous and possibly disastrous type.—I am, etc.,

H. LEHMANN.
St. Bartholomew's Hospital, London E.C.1.

Panic Immunization

SIR,—I have been following with keen interest the publication in the *Journal* on this subject (the article by Dr. Guy Bousfield (July 1, p. 43), and the letters by Dr. E. J. Moynahan and Dr. A. R. Broadbent (July 15, p. 173)). Recently I have come across a panic caused by a small rise in paralytic poliomyelitis in a restricted area in one State (Andhra Pradesh) in India. The situation demanded quick but definite action and answers to some questions similar to those already discussed by your correspondents. In March a letter was received from the Director of Public Health of that State stating that since February paralytic polio was being noticed on a scale larger than in the previous years. The Polio Research Unit of the Indian Council of Medical Research got busy and elicited facts on the epidemiology, and found that the incidence was 0.2 per 10,000 of the population and the age group involved was below four years with a peak at two. But the most surprising part

was the awareness of the population to polio vaccine. Crowds gathered outside vaccine-giving centres and there were generally long queues.

It was a typical panic. At that very time there was mass vaccination against smallpox going on throughout the State, and the question of simultaneous immunization against smallpox, using the customary vaccination and oral polio vaccine, had to be decided on. On scientific grounds, and fortified with an opinion from Dr. Sabin, both these were allowed to go on simultaneously. The question of immunizing the few stray children who had recent Salk vaccine and triple antigen had also to be answered. In some parts of the State cholera broke out, thus adding to the complexity of the problem. Fortunately, taking all these into consideration and facing what may have been unnecessary fears of reactions, a child population of over 100,000 (aged 2 months to 5 years) was immunized with triple live virus oral vaccine (Sabin).

The vaccine was given after medical check-up and under medical supervision. The necessary staff came from the Department of Public Health, and medical officers from the State. The Polio Research Unit of the Indian Council of Medical Research did the planning, training, etc. Written consent of the parent was obtained in every case. Occasional reports of mild reactions were received but none would come to the status of alarming. No genuine cases of allergic reactions were noticed.

One interesting matter needs careful thought. Penicillin is being used in the production of smallpox vaccine and polio vaccine. This opens the question of sensitization. In my experience there was no genuine case of this either. It is true that under panicky conditions quick decisions and firm actions are demanded. It would therefore be correct to say that susceptible populations must not be denied the benefits of immunization.—I am, etc.,

Polio Research Unit,
Indian Council of Medical
Research, Bombay.

P. V. GHARPURE,
Officer-in-charge,
Polio Research Unit, I.C.M.R.,
Grant Medical College,
Bombay 8, India.

Early Maturing and Larger Children

SIR,—The problem of the early maturing of children in many advanced countries (August 19, p. 502) must be seen in all its ramifications. In addition the mirror-image of the problem, that of the late maturing of children in underdeveloped countries, such as those of Africa, must be studied. It will be necessary to examine the changes which have occurred in the bigger children, including the chemical changes, the improvement in physical health, and also the possibility of earlier mental and emotional development. Not all of this may be found to be advantageous. Thus if the desire to mate falls below a certain age it may interfere with scholastic education. It may be found that rapid development contributes to certain psychological and social problems. Thus it might play a part in the increase of juvenile delinquency.

Another aspect of the problem is ventilated in a recent book of mine[1] on the incidence of non-infective diseases in Africans. Most African children grow at the same rate as European children and are the same size during the first few months of life, but from the age of 6–12 months—that is, usually after weaning from the breast—they fall behind and grow slowly throughout the whole of childhood, until they become adults who are probably smaller than they might have been if they had been better fed. However, among these African adults certain non-infective diseases are uncommon, at least as compared to Europeans of the same age and sex or indeed their descendants, the coloured folk of the United States.

Environmental factors, including that of diet, must be postulated to be operating in Africa, among whose indigenous inhabitants the following diseases are uncommon: (1) Severe degrees of atheroma of the coronary artery, coronary thrombosis, and angina of effort; (2) simple (postural) thrombophlebitis; (3) pulmonary embolism; (4) gall-stones, cholecystitis; (5) diabetes mellitus; (6) thyrotoxicosis; (7) rheumatoid arthritis; (8) osteitis deformans (Paget's); (9) eclampsia; (10) lumbar disk lesions; and (11) diverticulosis. For many other non-infective diseases the evidence concerning incidence in Africa is inadequate.

Other factors such as that of climate might play an important part. Thus disseminated sclerosis has as yet not been detected in an African, but it is known that this disease is less common in warm climates. The sites of cancer are sometimes different in Africans. Thus there is a low incidence of cancer of the stomach, colon, rectum, and gall-bladder, but a high incidence of primary cancer of the liver. On the other hand, certain degenerative diseases which are common in African adults are rare among Europeans—periportal fibrosis of the liver and endomyocardial fibrosis.

It is necessary to consider the chemical aspects of this problem—the alterations in the African *milieu interne*, the soil in which certain diseases thrive while others languish. Workers at university centres in South Africa have examined adult Africans and South African whites, both resident at the same place and time: they were far removed from the tropics. Employing the same techniques, these workers detected statistically significant changes in the two groups, matched in age and sex, with respect to the following constituents of the blood: cholesterol, albumin, γ-globulin, fasting blood sugar and the sugar tolerance curve, magnesium, uric acid; also in clot-lysis time and residual prothrombin time and in the urinary oestradiol. The evidence, admittedly very incomplete, is that certain of these chemical changes have not been detected at birth but are acquired probably early in life. The evidence suggests that the diet offered from early in life may play an important part. In this altered *milieu interne* certain diseases appear easily but others with great difficulty.

May I be allowed to make a suggestion concerning one of the dietetic factors which might be responsible? Milk, a food designed to grow the calf towards maturity in two years, has been taken in increased amounts in Britain since the agricultural revolution in the late 18th century, even more so during the present century. At present milk is taken in low amounts in underdeveloped countries: they would benefit by taking more. Whether we would benefit by taking less is unknown, but should be envisaged as a possibility.—I am, etc.,

Stratford-sub-Castle,
Salisbury.

HUGH TROWELL.

REFERENCE

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Gas Gangrene from Adrenaline

SIR,—In the leading article on gas gangrene from adrenaline (March 11, p. 730) it is stated that the earlier literature on the subject was almost exclusively Continental and four further examples have been reported from Australia, so the following case may be of interest to your readers.

In 1945 a healthy athletic young man of 23 was given an intravenous glucose injection for mumps. Within a few

minutes the patient had violent shivering, so an adrenaline injection was given in the upper left arm at about 6 p.m. The syringe was hurriedly sterilized by washing it out with spirit. By 11 p.m. the patient became severely ill with high fever and swelling. My second surgeon was sent for and he did not bring the patient back before 5 a.m., a distance of 43 miles (69 km.) over bad roads. I saw the patient at 6 a.m. A big dose of gas-gangrene serum had already been given, but in the meantime the swelling had spread to the chest wall. However, I gave permission to use up all the available penicillin, amounting to only a few million units. (In those early days of the drug, its administration was controlled.) The patient, however, died at 1.30 p.m.—that is, 19½ hours after the adrenaline injections. I had never understood the reason for the severity of this reaction. Now I know.

I had seen many cases of gas gangrene in France during the first world war, as I was one of the surgeons in the 1,400-bed general hospital in Boulogne, but never one of such severity.—I am, etc.,

Ranchi, India. A. N. PALIT.

Chloroquine and the Eye

SIR,—I would like to support Dr. A. H. Osmond's plea (July 15, p. 177) for care in the use of chloroquine, etc., and to congratulate the artist on the excellence of his drawing of the corneal changes. These latter were *exactly* as he depicts them in an elderly patient of mine who developed a skin condition diagnosed by a Johannesburg dermatologist as mycosis fungoides (reticulosis). He prescribed tab. "camoquin" (amiodiaquine hydrochloride) 1 b.d. and tab. "plaquenil" (hydroxychloroquine sulphate) ½ b.d.

In June, 1956, the patient's eyes were completely normal except for hypermetropic presbyopia. A year later he arrived at my rooms very distressed with painless blurred vision and complaining of seeing halos round street lights. The corneas were hazy, but there was no rise of tension and thus far no specific pattern to the corneal haze. I put him on miotics as a precautionary measure, and saw him daily. Ten days later I made a sketch of the typical striate keratitis pattern as described by Dr. Osmond and made the note: "Definite bilateral corneal striate keratitic haze, fan-like, with centre of fan below pupillary centre, striae vertical centrally and radiating outwards until horizontal laterally; *not* due to tension—? quiet toxic keratitis—? ? fanlike corneal dystrophy."

The patient's general practitioner could find nothing to suggest a toxaemia, and I suggested that the drugs he was on might be the cause. We wrote to the dermatologist, who seemed doubtful, but it was decided to stop the drugs. Six weeks after this the corneas were quite clear and vision with correction was again 6/6 in each eye, a dramatic change from the "hand-movements only" of a few weeks back. Six months later he complained that the "mistiness was starting again" and informed me that he was again on the tablets, as they had helped his skin condition. Within a week or two the typical fan pattern reappeared, only to disappear a month or so after discontinuing the tablets. There were no obvious retinal or macular changes after the two attacks, and the eyes were "quiet" throughout.

The recurrent pattern of the striate keratitis is of interest, as it suggests the presence of a constant tissue-space architecture in the subepithelial region. The striae were visible in the epithelium and in the vicinity of Bowman's membrane, and seemed to go deeper into the substantia propria but became lost in the general haze. There was never any suggestion of a breakdown or bullae in the epithelium.

In January, 1960, when I last saw the patient, his eyes were normal in all respects.—I am, etc.,

East London, Cape Province, South Africa. C. J. BLUMENTHAL.

Diagnostic Cytology

SIR,—Drs. J. G. S. Crabbe and Mary E. Egerton (June 24, p. 1790) are to be congratulated in their attempt to awake interest in diagnostic cytology in the United Kingdom. This subject has been neglected over the years in spite of the excellent work and publications of Anderson, Bamforth, Crabbe, Schade, Wachtel, and others. The present authors, however, by quoting chiefly from British publications, appear to have weakened their arguments to an apologetic plea.

The best weapon we have to date against cancer is early diagnosis. Cytology has fast become an exact primary diagnostic weapon. It is no longer the mere study of exfoliated material as such, but rather a sensitive viewing of tissue as mirrored in its component cells when smeared out on a slide. Screening involves a conscious attempt at the resynthesis of the tissue of origin, a task not to be delegated to routine, but requiring specialized training and a uniform technique.

In the cytologic diagnosis of any cancer the number of false positive or negative reports depends largely on the experience of the observer. The suggestion that "it really does not matter which method" is used for the preparation and staining of smears cannot be too strongly deprecated. A uniformity of technique is essential if we are to benefit from the vast experience and knowledge of advanced workers in this field. Attention to fine detail is what makes for success in diagnostic cytology. Toward this end the Papanicolaou method of preparation remains the best for undistorted cellular features.

In the diagnosis of cancer of the cervix the importance of a direct cervical smear in addition to the usual vaginal aspiration must be emphasized. Many cancers will be missed if this is not done. The cytologic diagnosis of endometrial cancer is becoming more exact, and, thanks particularly to the work of Koss and Durfee,[1] is now well established.—I am, etc.,

Andrew Ricci Laboratory of Diagnostic Cytology, Bulawayo, Southern Rhodesia. F. G. FEINSTEIN.

REFERENCE

[1] Koss, L. G., and Durfee, G. R., *Diagnostic Cytology and its Histopathologic Appearances*, 1961. Lippincott, Philadelphia.

Silent Antepartum Rupture of the Uterus

SIR,—I was interested in the case report by Mr. W. Gordon Millar (July 22, p. 218) of rupture of the uterus at 34 weeks' gestation without labour having commenced. That this is, as he suggested, a far more common condition than one is apt to suspect has, I think, been shown by the *Rotunda Hospital Reports* over the years since their first publication. In a paper read before the Canadian Society of Obstetricians and Gynaecologists, and shortly to be published,[1] I have extracted cases of rupture of the uterus in previously apparently undamaged uteri and compared them with rupture of the uterus occurring as the result of previous hysterotomy, and have found that out of 141 ruptured uteri in this 68-year period only twelve ruptures were through a caesarean scar.

In his comment Dr. Millar wonders "if an unrecognized incomplete rupture at the time of a previous delivery might have been the cause in some of the recorded cases of silent antepartum rupture of the uterus." G. FitzGibbon[2] mentions this factor in the multiparous patient, and in my experience I am aware of at least nine cases where a quiet rupture of the uterus had occurred at about 36 weeks' gestation without necessarily any gross physical signs at the time of the rupture. In cases where the patient has survived rupture of the uterus, subsequent cross-examination with regard to her immediate preceding pregnancy will usually reveal that after possibly a long first stage "a pain not like a proper labour pain affected delivery." FitzGibbon suggested that this was an incomplete rupture of the uterus, and that had labour needed to continue subsequent to this contraction the uterus would have completed the rupture at that time.

In three cases where the condition of rupture was recognized prior to labour it was found that the cervix was well taken up and applied and more than three fingers dilated at the 34th to 36th week of pregnancy, without there having been any suggestion of labour contractions. Unfortunately, in one of these cases the true state of affairs was not recognized, and on the exhibition of "pitocin" to hasten her supposed labour she completed the rupture and died rapidly of shock and haemorrhage in a nursing home, where operative facilities were not available. However, this patient's demise served as a warning for the next patient who was seen fairly soon thereafter, and in her case, suspecting the condition, laparotomy was performed and the lower segment of the uterus anteriorly was found to consist of amnion, chorion, and peritoneum only. During my assistantship in the Rotunda Hospital a case was admitted of a multipara at 36 weeks' gestation in whom the cervix was dilated about half without there having been any labour pains, and on vaginal exploration the feeling was that, on passing the fingers through the open cervix, one came rapidly upon the inside of the anterior abdominal wall. Laparotomy confirmed this finding. The patient had not at any time been shocked, but had come in because she said she did not feel right. The baby was still *in utero* and survived.

Unfortunately in some cases, in which the patient, having had no obvious trouble or difficulty in other pregnancies, has neglected to attend for antenatal care satisfactorily and is first seen in a state of shock immediately after delivery, the rupture has already completed itself. This is the type of patient that is seen by the emergency maternity unit in a state of irreversible shock or death.

These cases are extremely worrying and disturbing when encountered. But the writing is on the wall for those who take a careful, detailed obstetrical history and evaluate the pelvis and the state of the cervix during the last trimester of pregnancy.—I am, etc.,

Brantford, Ontario. H. FITZGIBBON.

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Post-operative Urinary-tract Infection

SIR,—In your leading article on the prevention of infection in the urinary tract (August 26, p. 571) you drew attention to the hazard of indwelling catheters following gynaecological operations. Their use is almost universal following operation for repair of the pelvic floor with or without vaginal hysterectomy, particularly if the bladder neck has been elevated to cure stress incontinence. We have demonstrated, in work to be published more fully elsewhere (Third World Congress of Obstetrics and Gynaecology), that in these cases they are in fact better omitted. Their omission, however, is not sufficient in itself to prevent urinary retention and infection, and is only effective if part of a policy of positive post-operative care in which the traditional routine of vaginal packing, frequent swabbings, bladder drainage, and prolonged immobility is reversed.

A psychological as well as physical assessment of the patient, careful explanation of the rationale of early mobility, and training in pelvic floor, arm, leg, and breathing exercises with emphasis on early restoration of normal function must be an integral part of pre-operative preparation. Post-operatively patients are not given bed pans, except on request on the first evening, and catheterization is not carried out unless necessary. A single injection of "omnopon" gr. ½ (22 mg.) ensures sleep the first night, and subsequently the application of a local anaesthetic aerosol as required gives adequate pain relief in approximately 80% of the cases. The following morning—that is, less than eighteen hours after operation—the patient walks to the lavatory, even after vaginal hysterectomy, and usually micturates normally. Vaginal packs are not used and routine swabbing, which has little purpose except to make the patient even more conscious of her perineum, is not carried out.

The elimination of these routine procedures permits the nursing staff to observe their patients properly and give the sympathy and understanding which is so important in the care of these difficult cases.—I am, etc.,

Dudley Road Hospital, Birmingham 18. EDWARD COPE.

Cross-infection from Hospital Baths

SIR,—At this time when hospital design and the prevention of cross-infection are under general consideration one feature appears to have escaped attention. This is the design of ablution rooms. In this country there is a traditional respect for the bath for overall cleansing. It is not denied that frequent baths produce a high degree of social cleanliness; as a pre-operative ablution, however, the bath falls short of the ideal even if it is adequately disinfected between each individual's use. For this purpose the only satisfactory method is a spray, where the soiled water runs at once to waste and the only parts of the individual placed at risk to cross-infection from the previous user are his feet. It is difficult to understand why these are not installed in new buildings. The space required is halved, the requirement of hot water is not greatly altered, and the method of cleansing is similar to that regarded for many years as compulsory for the hands of all those directly concerned in operative treatment.—I am, etc.,

Bridge of Earn Hospital, Perthshire. A. IAN L. MAITLAND.

Pythagoras and the Beans

SIR,—For a number of reasons the significance of the Pythagorean prohibition of beans may be questioned. Dr. George Discombe (August 5, p. 385) has mentioned two: that Aulus Gellius claims that Pythagoras frequently ate beans, and that his warning was against venereal excess and not against favism. Plutarch[1] gives another interpretation: "This duty Pythagoras also has enjoined in the form of allegories which I shall now quote and explain. . . . Abstain from beans means that

a man should keep out of politics for beans were used in earlier times for voting upon the removal of magistrates from office."

If Arie[2] is correct in his suggestion that the origin of the taboo lies in the prevalence of favism in Mediterranean lands, one might expect to find other comment on this. Hippocrates[3] was unaware of the association of beans and disease and wrote: "Beans afford an astringent and flatulent nourishment; flatulent because that the passages do not admit the abundant nourishment which is brought, astringent because that it has only a small residue from its nourishment." Cicero[4] said much the same thing: "For this reason, it is thought, the Pythagoreans were forbidden to indulge in beans, for that food produces flatulence and induces a condition at war with a soul in search of truth." There is biblical reference to beans (2 Samuel, xvii, 28, and Ezekiel, iv, 9) but there is no indication that they may cause illness. The bean was a staple article of diet in Mesopotamia and in Egypt and was used in the materia medica of these two countries.[5]

On the present evidence it seems best to accept the view of Sansone, Piga, and Segni[6] that the first report of favism is that of Manuel Pereira de Mira Franco, of Portugal, in 1843.—I am, etc.,

Wilmslow, Cheshire. IAN BAILEY.

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1 Plutarch, *De Liberis Educandis*, 17.
2 Arie, T. H. D., *Oxford med. Sch. Gaz.*, 1959, **11**, 75.
3 Hippocrates, *Regimen*, II, 45.
4 Cicero, *De Divinatione*, I, 30.
5 Sigerist, H. E., *A History of Medicine*, 1951, vol. I, pp. 249, 340, 402, and 485. Oxford University Press, New York.
6 Sansone, G., Piga, A. M., and Segni, G., *Il Favismo*, 1958. Minerva Medica, Torino.

SIR,—Dr. George Discombe (August 5, p. 385) rightly says that the reason why Pythagoras forbade his disciples to eat beans was as much a mystery to the ancient writers as it is to us: their suggestions are all obviously guesses or rationalizations, and, though they make interesting reading, there is little reason to prefer one to another.

Recently some light has fallen on the problem as a result of the work of Szeinberg, Sheba, and their colleagues.[1] They have studied the various ethnic groups of Israel in order to discover the incidence of the inherited defect of glutathione metabolism in the red cells, which is now known to occur in people who are prone to favism and to certain other haemolytic sensitivities. Dividing their subjects into Ashkenazi and Sephardi Jews—that is, broadly speaking, Jews of central and eastern European origin on the one hand, and those of Mediterranean and Oriental origin on the other—they found that only the latter group was susceptible to favism and that among its members alone (with only one exception) was the characteristic biochemical lesion found.

Next they divided the Sephardis into subgroups according to their lands of origin, and they found that the Jews from Iraq had a greater incidence of the glutathione anomaly than any other group except those originating from Kurdistan and from Persia. Now, the Iraqi Jews have had more continuity and greater seclusion than almost any other Jewish community; indeed, they were driven into Babylonian exile by Nebuchadnezzar in 586 B.C. As I have pointed out elsewhere,[2] this is the very century in which Pythagoras flourished, and it is therefore a reasonable assumption that favism existed in the world of his day.

Did Pythagoras himself suffer from favism? There is evidence that, like many who suffer from favism, he could not bear to walk among beans. Accounts of his death[3 4] relate that when he was being pursued by the people of Croton he came to the edge of a bean field, and rather than set foot in it he was taken, and died at the hands of his pursuers. Whatever the germs of this story are we can take our choice whether we believe that he was stopped by religious scruple or whether he was nauseated by the bean blossom.—I am, etc.,

The Radcliffe Infirmary, Oxford. T. H. D. ARIE.

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4 Diogenes Laetrius, *Life of Pythagoras*, VIII, 39.

Schizophrenia in General Hospitals

SIR,—I agree with your correspondents (August 12, p. 453) that my impressions of the treatment of schizophrenia may be fundamentally misconceived. If equally critical of their own views, our differences are not as great as might appear. "A judicious distrust and wise scepticism are the sinews of understanding" (Epicharmus).[1] I can sympathize that anybody who has expended time and trouble to acquire a specialized technique would subsequently "prefer" to agree with evidence that it is useful. The danger, as I see it, is threefold.

Firstly, there is an understandable reluctance to discard such a skill, with all its accoutrement, ancillary staff, team spirit, and reputation, when no similar tangible physical ritual can be substituted. Secondly, enthusiasts tend to find spurious improvement resulting from their therapeutic exercises. Thirdly, genuine improvement may be attributed to treatment when due to other factors, as was the case in the plausibly deceptive conclusions drawn by Drs. Peter Rhode and William Sargant (July 8, p. 67) from study of their treatment of schizophrenia in general hospitals. Specious evaluation has been applied to so many remedies—bloodletting, tar water, malarial therapy, to name a few—that it is fascinating to read Penrose's objective study[2] of crazes, particularly thallium therapy.

I have no quarrel that larger doses than 5 mg. of trifluoperazine three times a day and other drugs may be necessary in some cases of schizophrenia. I agree that E.C.T. may be useful in some cases where depression is marked, but to say it is indispensable in these or catatonic stupor is more to make a point than propound a truth.

Seventy per cent. of cases of schizophrenia are not in psychiatric hospitals. They are being helped to stay in the community by their families and family doctors —many without drugs, and I doubt if more than a few have the high doses recommended. Before deciding on treatment one would not wish to have oneself, it behoves hospital psychiatrists to ask themselves how the patient has existed with his illness in the community for so long before admission. Often one finds there has been little change in the illness, but domestic, financial, or other social factors have been responsible for admission to hospital. It is much easier to write a prescription for a large quantity of drugs than provide community care correcting such factors. I am not willing to limit my therapeutic effort in any way, but when considering

the various approaches to the treatment of disease I think we should all bear in mind that we will not be suffering from the side-effects, the risks, nor footing the bill. Pinel wrote,[3] "My faith in pharmaceutical preparations was gradually lessened, and my scepticism went at length so far as to induce me never to have recourse to them, until moral remedies had completely failed."

However much our beliefs and impressions of treatment are biased by our personal needs, drug-firm persuasion, and the climate of contemporary opinion, we still have to explain the remarkable results obtained by Brown and Conolly in England, Todd, Woodward, and Butler in America, and others long before tranquillizers, barbiturates, deep insulin, E.C.T., and leucotomy were known.[4]—I am, etc.,

Severalls Hospital, Colchester. RUSSELL BARTON.

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Reversed-ear Syndrome

SIR,—I was most interested to read Surgeon Lieutenant Antony Jarrett's description (August 19, p. 483) of his experimental reproduction of the phenomena of "reversed ear" and his manometric measurement of the forces involved in its production.

In 1953, at the time that Cousteau was publishing[1] his views on "reversed ear," the concept of external auditory meatal "squeeze" haemorrhage—that is, haemorrhage from subcutaneous vessels underlying areas of skin wherever the ambient pressure transmitted through the tissue fluids, according to Pascal's law, was not supported by an equal localized pressure—was the concept held and taught in the Navy. Dr. Jarrett's idea of the drum being perforated through outwards (by explosion of air from the middle ear) just did not happen, and the bullae occurred far more frequently over the bony external meatus than on the outer surface of the drumhead itself. These cases of bleeding from the ears caused by external auditory "squeeze" by the vented soft rubber hood were treated as relatively superficial injuries, and little time was lost from diving because of them.

Although the theoretical requirements for the avoidance of these injuries was well understood, the practical application of these desiderata to every circumstance of flexible-hood diving was not so easy to achieve. Dr. Jarrett's solution has been the surrender of the older ideal of waterproofed isolation from the cruel sea in preference for its more intimate but more gentle embrace through suits of porous material.

Shall our space-suits be porous too? I can imagine Mr. Kennedy's first lunar explorer in 1971 regarding with dismay his subungual ecchymoses as he pulls on his cuffed, flexible glove in order to write home his first letter describing the syndrome of "reversed hand."—I am, etc.,

Melton Mowbray, Leics. H. HOLLIS.

REFERENCE

1 Cousteau, J. Y., *The Silent World*, 1952, Hamish Hamilton, London.

Orange-bolus Obstruction

SIR,—In view of the frequency of gastric operations, the following case of spontaneous resolution of orange-bolus obstruction after partial gastrectomy may be of interest.

A male of 42 years was admitted with epigastric pain of 24 hours' duration. The pain was a constant, dull ache, with exacerbations every 5 to 10 minutes, lasting one to two minutes, gradually moving down to the umbilicus. He had vomited more than 20 times in the 24 hours. In 1957 he had a Polya partial gastrectomy for duodenal ulcer.

Examination: tongue furred brown. Pulse 80. Temperature 98° F. (36.7° C.). Abdomen—slight central distension, tender at umbilicus and right iliac fossa. Erect *x*-ray of abdomen revealed distended small intestine, with fluid levels. Urgent laparotomy was considered and he was reviewed at hourly intervals.

Severe colicky pains persisted, associated with nausea and sweating, gradually moving to a sub-umbilical position. Five hours after admission he had a compelling urge to defaecate, and a large bolus, 8 cm. × 5 cm. × 5 cm., was passed. This consisted of an undigested, matted mass of orange fibres. He had no further pain or vomiting. Upon closer questioning, he recollected that three hours before the onset of the pain and vomiting he had "swallowed an orange almost whole" when someone slapped him on the back.

The importance of inquiry about eating oranges is stressed in late intestinal obstruction after partial gastrectomy. An orange bolus may be passed spontaneously and immediate surgery is not necessarily indicated, provided that the diagnosis can be made, the obstruction is at an early stage, and the bolus appears to be passing onwards as judged by the level of referred visceral pain.

The passage of a bolus of this size is worthy of note. Latchmore[1] describes a case where enterotomy was necessary to remove a bolus of orange segments 2½ in. × 1 in. (6.3 cm. × 2.5 cm.).[2] Cooper describes intestinal obstruction in a case where only two segments of orange were present. In 1957 Spurzem and Desser[3] found only 12 cases of intestinal obstruction due to phytobezoars following gastric resection. Oranges were the most common cause.

I would like to thank Mr. A. J. C. Latchmore for kind permission to publish details of this case.

—I am, etc.,

Horsforth, near Leeds. P. M. BINNS.

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Headache and "Eyestrain"

SIR,—It is with some concern that I write in regard to the letter of Dr. W. S. Inman (July 15, p. 178), since he states ophthalmologists are in confusion about their practice. I will agree that "headache" is capricious, but if it is the only symptom then it certainly can be a visual problem.

There exists a most mysterious visual defect which is not only little known to the public but to the "older" ophthalmologists as well. Headache is the chief symptom, among the other eye symptoms, in the condition called aniseikonia. As testing methods improve this condition becomes more and more common. Aniseikonia results when each of the two images are of different sizes and a persistent binocular

failure results. The eye must produce almost identical images before the brain can blend them into a single and accurate visual impression; as little as ½% difference in size can be of dire discomfort to the patient. Those of us experienced in cataract extractions and operations for prosthetic lens implants are only too familiar with this troublesome problem. Again, new glasses which are absolutely a proper correction will change image sizes and produce a "false" aniseikonia until binocular vision becomes readjusted. Although aniseikonia has been known for some years, the experience and complex equipment necessary to diagnose a case made it impractical for even those of us with extensive ophthalmic practices. Fortunately, recent improvements have made it possible to perform these tests on a much simpler device.

It is often possible to compensate differences in image sizes, up to a point, in the two eyes by proper choice of the types and geometric curves of ordinary spectacle lenses. Usually it takes a very special lens—an "isokonic" lens—to correct the condition. These lenses magnify the image for one eye just the right amount, averaging from ½% to 5%, to equalize the images. An important point to remember is that an aniseikonic headache can exist in a patient with apparent emmetropia—it requires an ophthalmo-eikonometer to discover the latent abnormality—hence it is conceivable that a correction of 0.125 D astigmatism can alleviate the headache if under the ½% variant.

I do not propose to enter into counter-arguments with Dr. Inman, but my file contains a goodly number of cases representing grateful patients who carry eikonic correction, and who are quite happy and comfortable with this "potent magic"; now, what happened to all these headaches?—I am, etc.,

Saint Martins, N.B., Canada. W. L. COOPER.

Aids for the Blind

SIR,—Through the Health Service our Welfare State has provided hearing-aids for the deaf, trusses for the ruptured, spectacles for the myopic, wigs for the bald, chairs for the lame, and many other such aids to reduce unhappiness.

The blind, however, still seem to be singularly dependent upon the charity of their fellows, despite the fact that they are among the most heavily afflicted. Is it not time that the Health Service provided them with radios and with guide dogs and any other of the aids which have been developed for them?

This should be done either directly or by generous grants to the numerous organizations that have so valiantly struggled to help these people. If this were done there would still be room for those who wish to offer charity, and their gifts could go towards gramophone records and other "necessary" luxuries.—I am, etc.,

Birmingham 15. GEORGE T. WATTS.

Antimony and the Heart

SIR,—We have just received the *Journal* of July 8 and are particularly interested in the letter (p. 108) on antimony and the heart by Dr. O. D. Standen.

We are in a hyperendemic area of *Schistosomiasis mansoni* and have been treating cases of this condition for twenty years with either potassium or sodium antimony tartrate in the main. Most of these cases have been treated as out-patients for lack of in-patient accommodation. Because of the cardiac and other toxic effects of antimony compounds we have gradually evolved a few cardinal principles of treatment designed to minimize these, which are:

(1) To give treatment to those patients only who have a positive stool examination, without using concentration methods, and who have definite symptoms for which no other cause can be found. (2) To give treatment according to the following regime: Gradually increasing dosage of sodium antimony tartrate intravenously up to a maximum of 1 gr. (65 mg.) per dose and frequently not more than ¾ gr. (50 mg.). This dosage to be given twice a week only, not the usual three times a week, but be continued for six weeks. (3) Never to give more than two courses of treatment to one individual. It is better to remain infected than have more antimony.

Our experience seems to indicate that the length of time over which treatment is given is more important than the dosage of antimony given. We feel that six weeks is the minimum period, and hope to find that dosage as low as ½ gr. (32 mg.) twice a week will be adequate. Schistosomiasis seems to be an innocuous infection in many people but always constitutes a danger in any individual who becomes ill for any other reason. Many cases of schistosomiasis with symptoms date these symptoms from an intercurrent illness. This subject is of absorbing interest to many. I trust there will be further correspondence.—We are, etc.,

Kuluva Hospital, Arua, Uganda. E. H. WILLIAMS. PETER H. WILLIAMS.

External Cardiac Massage

SIR,—Your cautionary annotation on external cardiac massage (August 12, p. 440) does not altogether answer the problem presented to the first-aider by a case of cardiac arrest. He cannot expect to have a doctor always on call at 3 minutes' notice to make the diagnosis for him. He will therefore find it necessary to make the diagnosis for himself, based on the corpse-like appearance of the patient, who is unresponsive to stimuli, with absent breathing, impalpable radial and carotid pulses, and motionless, forward-looking eyes with equal pupils unresponsive to light. If this condition is maintained for half a minute the diagnosis of cardiac arrest can be regarded as reasonably probable.

External cardiac massage subserves two related but quite dissociable functions. Your annotation deals with its role in maintaining the circulation. The other function, which may be more important in relation to cases seen outside hospital, is that of mechanical stimulation of the arrested heart. In each of my three cases three or four firm pressures over the front of the sternum, as required for external cardiac massage, sufficed to re-establish the heart-beat. (Reconstruction of these incidents suggests that the duration of cardiac arrest was about 25 seconds, 35 seconds, and 130 seconds respectively.) Cases of this kind are not uncommon, and should be easily within the competence of an instructed first-aider.

Prolonged external cardiac massage with mouth-to-mouth breathing may be a more daunting procedure, but it would be unrealistic to imagine that it will never be attempted by the layman—the mother who has seen her child electrocuted, for example—and our hospitals should be equipped to deal with such cases.—I am, etc.,

Lowestoft. N. B. EASTWOOD.

Insertion of Intravenous Cannula

SIR,—Dr. C. K. Jones's comment (August 12, p. 456) on the insertion of an intravenous cannula is relevant to a technique of percutaneous infusions which is not universally appreciated by house officers. This is to insert the hollow needle of a giving set until there is no "redundant needle" outside the skin.

To achieve this in the majority of cases it is essential to have the needle connected to the infusion bottle, so that when it punctures the vein there is a continuous column of fluid from the vein to the bottle. The vein therefore does not collapse, and the needle can be pushed along the dilated lumen to its hilt. With this length of needle in the vein there is much less chance of the point piercing the wall again, as the needle tends to move *with* rather than *across* the vein. When well set up I venture to suggest that such a drip will run as long as it will through a cannula, and in the case of a forearm vein splinting is not necessary.—I am, etc.,

Saint Catherine's Hospital, Birkenhead, Cheshire. D. A. S. MARTIN.

Pulmonary Tuberculosis and Pregnancy

SIR,—Drs. Ronald B. Pridie and Peter Stradling are to be congratulated on their article (July 8, p. 78) because they have reminded us that the great changes wrought by chemotherapy in the treatment of tuberculosis in the general population apply equally to the pregnant and the parturient.

Prophylactic therapy is also available to the newborn infants, and Drs. Herbert Barrie and B. D. R. Wilson, in their letter of August 26 (p. 580), have not mentioned this fact. They are assuredly right in saying that from the paediatric viewpoint exposure of the newborn to contact with pulmonary tuberculosis is wholly unjustifiable, but there is no risk in exposing a *protected* infant, and isoniazid is a potent protector easily administered and willingly accepted from birth onwards. Its efficacy has been clearly shown by Dormer and his colleagues.[1] Although it is true that the administration of isoniazid can only defer the period of segregation, the interval which it covers may prove invaluable. Drs. Barrie and Wilson will appreciate the risks of segregating newborn infants for six weeks; it is almost inevitable that some will succumb to nosocomial infections.

A better protection, obviating segregation entirely, may be provided by starting isoniazid therapy immediately after birth and concurrently vaccinating with an isoniazid-resistant B.C.G. vaccine, as was described by myself and Dr. Margaret I. Griffiths in the *Journal* of May 27 (p. 1500). Drs. Barrie and Wilson stress the need for teamwork, and it is indeed essential. The chest physician, in the light of his knowledge of the state of her infection, will pronounce on the mother's capabilities; the obstetrician will determine the safest method of delivery; and the paediatrician will see that isoniazid is immediately forthcoming for the infant—unless the chest physician has told him that the mother's infection is with an isoniazid-resistant organism, in which case arrangements for segregation *must* be made.—I am, etc.,

Manchester 13. WILFRID GAISFORD, Vice-Chairman, Joint Tuberculosis Council.

REFERENCE

[1] Dormer, B. A., Harrison, I., Swart, J. A., and Vidor, S. R., *Lancet*, 1959, **2**, 902.

Latent Brucellosis in Farmers

SIR,—In their article on subclinical infection with *Brucella abortus*, Drs. Ian McWhinney and A. P. Prior (July 8, p. 80), unfortunately state "it is evident that a titre of up to 1 in 320 is of no diagnostic value in a farmer." Barrett and Rickards described[1] chronic brucellosis in 25 patients. Among them were 16 with titres of 1/240 or less, and 8 of these were farmers in 3 of whom the agglutination tests were negative. In Ireland chronic brucellosis may be found in the presence of dilutions below 1/320.[2] The titre of each individual case must remain a tentative laboratory aid which should be viewed against the background of clinical and other findings. If titres of 1/320 or less are ignored, many patients will remain in unnecessarily prolonged misery.—I am, etc.,

Galway, Ireland G. E. HEWSON.

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[1] Barrett, G. M., and Rickards, A. G., *Quart. J. Med.*, 1953, **22**, 23.

[2] Hewson, G. E., *Trans. ophthal. Soc. U.K.*, 1955, **75**, 229.

Fusion of Labia Minora

SIR,—I have followed the correspondence on this topic with interest, having encountered the condition on one occasion. The patient, a spinster of 82, complained in 1956 of pain and difficulty in micturition. On examination, there was almost complete fusion, and the urine was voided slowly through a pin-hole meatus at the anterior end. She was admitted to hospital, where the labia were separated by probes and blunt dissection, and a nitrofurazone gauze pack was left in position for a few days. The labia healed perfectly, and she has experienced no trouble since that time.—I am, etc.,

Kingston-upon-Thames, Surrey. GWILYM EVANS.

A Matter of Style

SIR,—I write to plead for better orthography in your journal, please. In your annotation, "Barotrauma of External Auditory Canal" (August 19, p. 507), Eustachian tube is spelt with the minuscule "e." This flagrant solecism appears also in the article pertaining to the same subject on page 483. If this is allowed to go on unchecked we may progressively have to read and endure babinski's sign, hunter's canal, benedict's test, and so on. This letter is not written in captious or carping criticism, nor is it pedantic; it is prompted only by the hate of seeing the beauty of the English language destroyed by careless writing.—I am, etc.,

London S.W.19. B. J. BOUCHÉ.

*** After putting on his macintosh and wellingtons he ate a sandwich, picked up his gladstone bag, and took the macadamized highway to Glasgow in order to boycott the English. Isn't this beautiful?—ED., *B.M.J.*

Post-myocardial-infarction Syndrome

SIR,—In their most interesting article on this subject (August 26, p. 535) Drs. Chalmers Davidson, M. F. Oliver, and R. F. Robertson rather surprisingly do not mention acute non-specific ("benign") pericarditis in the differential diagnosis. That this disease is probably much more common than the post-myocardial-infarction syndrome is suggested by the fairly large number of published cases. I was able to collect fourteen in some ten years,[1] and I am unable to recall with certainty any case of the post-myocardial-infarction syndrome in a very large number of cases of cardiac infarction. I feel

that the incidence of 4% claimed by Dressler[2] does not apply in this country and that the figure of 1% suggested by Drs. Davidson, Oliver, and Robertson is probably nearer the truth for us.

The relapsing course of acute non-specific pericarditis, its associated pleural and pulmonary involvement, and its favourable response to steroid therapy suggest that the same mechanism is at work in this disease, in the post-myocardial-infarction syndrome, the post-commissurotomy syndrome, and in the late complications of direct trauma of the heart[3], and that this mechanism may well be an autoimmune reaction.—I am, etc.,

Newcastle upon Tyne 7. W. G. A. SWAN.

REFERENCES
1 Swan, W. G. A., *Brit. Heart J.*, 1960, **22**, 651.
2 Dressler, W., *Arch. intern. Med.*, 1959, **103**, 28.
3 Wood, P. H., *Diseases of the Heart and Circulation*, 2nd ed., 1956. Eyre and Spottiswoode, London.

Oral Contraception

SIR,—I share Dr. Gabriel V. Jaffé's enthusiasm (July 8, p. 112) for the possibility of a safe, easy, and effective method of oral contraception. I do not agree that oestrogens in sufficient quantity to prevent ovulation are not causing an upset in hormone balance.

The facts I endeavoured to establish in my letter were: (1) That the administration of oestrogens for long periods except under close medical supervision might be risky. The three hormones in general use—thyroid, insulin, and the cortisone group—all produce iatrogenic disease even under medical observation. (2) That oestrogen summation disease does occur in other mammals. (3) That one of the complications in sheep is permanent sterility (and this can occur with very few general signs). (4) The signs of acute oestrogen disease are detectable and abate when the hormone is withdrawn, but the subacute condition is difficult to diagnose and not reversible. (5) Different animals, and even different breeds of the same animal, show varying degrees of toleration.

Possibly the human is immune, but it would take about 15 years of careful study to be certain of this. I feel that the safety of the individual is the prime factor governing advice on contraception.—I am, etc.,

Wongan Hills, Western Australia. T. LOVEGROVE.

Shortage of Nurses

SIR,—Dr. D. H. Barham (August 5, p. 384) suggests that if the principle of accepting only Government-sponsored applicants from Ghana and (I quote) "other underdeveloped countries" were waived a great contribution would be made to the solution of the problem of nurse shortage in the United Kingdom. It is true that this would undoubtedly mean a great influx of candidates for training, especially from countries which, unlike Ghana, place no restrictions upon would-be emigrants. But the point of the principle is selection—i.e., to try to ensure that only those capable of successfully completing the course for State registration are given vacancies for it.

There is a great deal of bitter disappointment among those who come (and some do) without official recommendation and who, on arrival, either cannot get vacancies because they are not up to the required standard or who are given a chance and find for themselves that the course is beyond them. True, if their failure is in theoretical work only and they are temperamentally suited to nursing, they can take the course for enrolment, but again they face frustration on their return home, since that qualification is not at present recognized outside the United Kingdom. Also, since most wish to obtain State registration only so that they may return to better posts in their own countries, they would help here only while student nurses. They might also find that there was no suitable employment for them at home when qualified.

It would appear that the Ghanaian Government is doing its best to protect its citizens from unhappiness and distress by requiring evidence of guaranteed employment and financial security before granting passports, and the policy adopted by many hospital authorities in the United Kingdom has the same objective.—I am, etc.,

LILIAN M. DARNELL,
Secretary,
Nursing Recruitment Service,
King Edward's Hospital Fund.
London W 1.

Abdominal Wound Dehiscence

SIR,—The cases quoted by Mr. A. W. G. Weir (August 19, p. 520) all had lower abdominal incisions and may also have been supported by tension sutures, while those of Mr. H. A. Kidd's series (July 15, p. 173) were restricted to upper abdominal incisions. The technique used in Mr. Kidd's unit has been the same for many years and is no less meticulous than that employed by Mr. Weir. All the cases quoted occurred in a three-month period and the operations were performed by three surgeons of considerable experience. The important factor was the absorption and fragmentation of the catgut within a period of 10 days. One thousand four hundred operations have been performed each year for the last 12 years and the incidence of dehiscence had been low until the three-month period under review.—I am, etc.,

Carshalton. B. P. FLANNERY.

Marjory Warren Memorial Fund

SIR,—The British Geriatrics Society initiated and is supporting a fund to commemorate the pioneer work of the late Dr. Marjory Warren, consultant physician in geriatrics at West Middlesex Hospital, Isleworth, who was killed in a car accident in September, 1960. The object of the fund will be to finance scholarships, tenable in this country or abroad, to promote the study of the medical, nursing, or social aspects of care and treatment of the elderly.

Dr. Warren, who was renowned not only in this country but in many countries overseas where she had lectured, advised, and helped, had in her lifetime effected a revolution in the attitude towards the older patient in hospital and enabled many to be given the opportunity hitherto denied of "making the most of their capabilities within the limits of disability."

Donations should be sent to Barclays Bank Limited, 54 Highgate High Street, London, N.6.—We are, etc.,

AMULREE,
President, British Geriatrics Society.
JOYCE COCKRAM,
President, Medical Women's Federation.
OLIVE A. F. DAVIS,
Chairman, South-west Middlesex Hospital Management Committee.
ALAN MONCRIEFF,
President, Institute of Almoners.

Obituary

RAFFAELE BASTIANELLI, M.D., Hon.F.R.C.S.

Professor Raffaele Bastianelli died on September 1 at the age of 97. One of Italy's great surgeons, he was honoured not only in his own country but wherever surgeons practise their craft. He was made an honorary Fellow of the Royal College of Surgeons of England as long ago as 1913, and a Foreign Corresponding Member of the British Medical Association in 1935. The 25th year of his professorship of surgery in Rome was commemorated in 1927 by a special number of the *Italian Archives of Surgery*, to which Sir Berkeley Moynihan, as he then was, contributed an article on perforating gastric and duodenal ulcers.

Professor Bastianelli was a general surgeon throughout the whole of his professional life, with a special interest in the surgery of the brain and the abdomen. During the war of 1914–18 he was in charge of a front-line surgical unit treating wounds of the head, the abdomen, and the chest. This remarkable man was one of the earliest qualified pilots in Italy, and for many years he flew his own aeroplane. The teaching and practice of surgery did not exhaust his exuberant vitality, which left him enough to spare to farm his own land and become a discriminating connoisseur of art. In a note published in the *Journal* on his ninetieth birthday we said: "His many friends in other countries will be glad to hear that old age has proved such a minor hindrance to one who was always noted for his intellect, open-mindedness, courage, and humanity."

Raffaele Bastianelli was born in Rome on December 26, 1863, the third of five sons. His father was head physician at the Santo Spirito Hospital, and came of Umbrian farming stock. His uncle was a surgeon in a small Umbrian city. After a classical schooling in Perugia and Rome Bastianelli entered the medical school of Rome University and took his diploma of physician and surgeon in July, 1887. Among his teachers were Francesco Durante, who in 1885 operated on an endocranial tumour, and Ettore Marchiafava, pathologist and malariologist, in whose laboratory Bastianelli worked for seven years. In 1889 he performed what was probably the first successful operation for a dermoid cyst of the mediastinum. Like all great surgeons who have made their mark Bastianelli travelled widely to extend his knowledge and experience, and in particular in the Anglo-Saxon world. The Mayo Clinic, the clinics of Crile and Cushing, the London Hospital, were among his favourite haunts, and he was an honoured friend of the great surgeons of his day in Britain and the U.S.A. Up to the age of 69 he continued to work as a surgeon in the hospitals of Rome, and after that in nursing-homes. When, a few years ago, he had to have an operation himself he gave clear instructions to the surgeon on how it should be conducted—a man who was one of Bastianelli's best pupils—and insisted on having the operation done under a local anaesthetic; he was out of the clinic in three days to be home again when his wife returned from holiday.

Professor Bastianelli received many honours from many countries. He was surgeon to the King and Queen of Italy and a Senator of the Kingdom of Italy until it became a republic.

MR. CLIFFORD MORSON writes: The announcement of the death of Professor Raffaele Bastianelli revived memories of the delightful meeting of the International Society of Urology held in Rome in 1924. Alessandri, professor of urology, was president of congress, and he had invited Bastianelli, who was a general surgeon not specially interested in diseases of the genito-urinary tract, to give a demonstration at his own hospital, the Policlinico. Bastianelli chose for his operation a case of tumour of the intercarotid body in a woman. He removed it under local anaesthesia, demonstrating to his audience the various structures in the neck which he revealed as he dissected out the growth. His surgical technique was masterly. At the end he received an ovation from an audience which included, besides your correspondent, Sir Walter Langdon-Brown, Sir John Thomson-Walker, Frank Kidd, and George Neligan.

Incidentally, the Policlinico authorities, on the advice of Bastianelli, had appointed an Englishwoman as matron a short time previously in order to improve the nursing.

D. P. HOLMES, M.D., D.P.H.

Colonel D. P. Holmes, medical superintendent of Rookwood Hospital, Cardiff, died at Llandough Hospital, Cardiff, on July 24, after a short illness. He was 59.

David Price Holmes was educated at Cardiff High School, Cardiff Medical School, and Westminster Hospital. After qualifying in 1925 and graduating M.B., B.S. in the following year, he was casualty officer and house-physician and then assistant pathologist at Westminster Hospital. He obtained the D.P.H. in 1929 and worked for some time as assistant medical officer to the Glamorgan county council. He left this post to become a medical officer in the Ministry of Pensions, joining the staff of Rookwood Hospital in 1937. As a Territorial Army officer he was regimental medical officer in the Royal Engineers and later in the Royal Corps of Signals, in which he became officer in charge of 35 Field Hygiene Section. In May, 1940, he accompanied the force which went to Iceland as deputy assistant director of hygiene. Here he undertook original research for his M.D. thesis on "The Health of a Northern Garrison." The conclusions he came to and the advice he gave in this thesis are still the basis for the protection of troops against cold climates and were applied in the Korean war. Several of the specialist appliances described have now become standard military equipment.

Colonel Holmes returned to Britain in September, 1941, and was deputy assistant director of hygiene, Salisbury Plain District. He was then appointed senior lecturer and colonel in charge of instruction in the Army School of Hygiene, Mytchett. At the end of the war, as a colonel, he was commanding officer of the 3rd Western General Hospital, and, having rejoined the Territorial Army, he was at the time of his death commanding officer of the 40th General Hospital and senior specialist in Army health in the Army Emergency Reserve. He returned to the Ministry of Pensions after the war, and after a year working in Manchester he became superintendent of Rookwood Hospital in 1947. Although this hospital is now one of the United Cardiff Hospitals treating civilians, there are still wards for Army pensioners.

Colonel Holmes's chief interest was in the health of the soldiers and the care of the old soldier. He wrote many papers on these subjects and on the history of artificial limbs, missiles, and types of casualties. He also wrote non-scientific articles, short stories, and plays, and was proud to be a member of the Savage Club. As a young man he was a rugby footballer, playing for Glamorgan Wanderers, of which club he later became the chairman.

He married the daughter of a Norwegian sea captain and she and two sons survive him.—A. L. J.

J. B. H. writes: South Wales, the West of England, and all his personal friends have suffered a very severe loss in the death of Colonel D. P. Holmes. He was indeed a man of many parts. At Rookwood he created a "very happy" hospital, and until his untimely death was a most efficient

and wise administrator, with always a very keen interest in the welfare of all ex-Servicemen, by whom he was universally loved. As a man, David, as we knew him, was a real pal. An "all rounder" in the cricket sense, he was keen on all forms of sport and always ready to lend a willing hand to those in need of it. His funeral service at Llandaff Cathedral was attended by a very large number of men and women who regarded him as a dear friend. He has left a very dear wife and two sons, one in the Royal Navy and the other at the University of London.

J. P. DAVIE, M.D., B.Sc.

Dr. J. P. Davie, who was until recently in practice in Chesterfield, died at his home there on August 7. He was 68 years of age.

James Paterson Davie was born on February 19, 1893, at Uphall Station, West Lothian. From Bathgate Academy he went on to the University of Edinburgh, where he first graduated M.A. and B.Sc. He used his scientific training to some purpose during the first world war, for he volunteered to serve in the Royal Navy and for a time was one of a team of research workers in antisubmarine defence. The war concluded, he returned to his old university, this time to study medicine, graduating M.B., Ch.B. in 1923 and proceeding M.D. in 1926. After gaining clinical experience in hospitals at Salford and Salisbury he started in private practice in Chesterfield, where in due course he also served as consultant physician on the staff of the Royal Hospital for a period of 22 years.

A. C. S. C. writes: It was with great regret that we, his fellow practitioners, heard of the death of Dr. James Paterson Davie. His final illness had been a long and distressing one, which he bore with much patience and courage. His failing health had necessitated his retirement from all practice in the year 1959.

In spite of a more than ordinarily busy professional life he found time to interest himself in civic affairs as a member of the Chesterfield Borough Council for nine years. He was, moreover, chairman of the Chesterfield Division of the B.M.A. from 1936 to 1937, and president of the Derbyshire Branch from 1947 to 1948.

His enforced retirement in 1959 was a great disappointment to all his patients, for whom he could never do too much. One feels that his more-than-busy life served to hasten his end.

He leaves a widow, two sons, both carrying on the family tradition as doctors, and three daughters.

S. S. DAVIDSON, M.R.C.S., L.R.C.P.

Dr. S. S. Davidson, physician to the London Clinic for Psycho-analysis, was drowned on August 7 while fishing in the River Spey. He was 50 years of age.

Sonny Sneir Davidson came to England from South Africa to study medicine at Guy's Hospital, where he qualified in 1938. He then went into general practice, and during the second world war he served with the R.A.M.C., when he became interested in psychiatry. After a short period of work in Northern Rhodesia as a medical officer in the then Colonial Medical Service, he returned to London. During his training at the Institute of Psycho-analysis he joined the staff of the Cassel Hospital, Richmond, and after eight years there he left to devote himself full-time to psycho-analytic work with adults and, later, with children.

B. J. writes: From early on in his psychiatric work Sonny Davidson showed a particular gift for understanding and treating extremely disturbed and psychotic patients. His desire to deepen this understanding may indeed be one of the factors which led him to the work of Melanie Klein, and he subsequently became one of her closest friends and colleagues. He participated keenly in the activities of the British Psycho-analytical Society, where he read occasional scientific papers, which it is hoped will later be published.

In his work, as in his life, Sonny Davidson showed certain striking characteristics—a basic integrity and a capacity to stand firmly by what he believed and to express his opinions fearlessly. But perhaps what stood out most clearly was his warm, tender, endless generosity; if a patient, colleague, or friend needed help he was always ready to give it, and would always stand by a person in need and see him through.

Sonny Davidson was a man who seemed really to enjoy life; he loved his work and he had many outside interests, such as the theatre and the arts—interests which were deeply shared with his family. He died at a time in his life when he had achieved much, but he had still so much to give, both personally and in his work as a practising analyst and teacher of psycho-analysis. It is a terrible loss for psycho-analysis, as it is for his family and friends. He leaves a widow and a son, who is now studying medicine.

KURT SAX, M.D., D.P.M.

Dr. Kurt Sax, who practised as a psychiatrist in Belfast, to which he came as a refugee from his native Vienna in 1939, died suddenly on July 27, aged 62 years.

S. R. C. R. writes: Kurt Sax was born in Vienna in 1899, and was the fourth generation of the family to practise medicine. He was educated at the Piaristen Gymnasium as a classical scholar. In the latter part of the first world war he was commissioned in an Imperial Cavalry regiment and served on both the eastern and Italian fronts, being awarded the Iron Cross. After the collapse of the Austrian Empire he began the study of medicine in Vienna. Graduating M.D. in 1925, he continued his studies in the Universities of Freiburg, Heidelberg, Bonn, and at the Sorbonne, and after the required five years was graded as gynaecologist and began practice in Vienna.

After the *Anschluss* and a period in a Nazi concentration camp he arrived in Northern Ireland as a refugee in June, 1939, to find that the "quota" for medical refugees had already been exceeded and that he could not be registered to practise in Britain. In consequence he returned to student life once more, this time in Belfast, where he graduated M.B., B.Ch. in the Queen's University in 1946, though he was granted temporary registration a year or two before this.

Viennese medicine during his early professional life was experiencing the ferment of the psycho-analytical, the individual, and the Jungian schools, and these had a profound effect on the young Dr. Sax. It was therefore natural that when he began to practise medicine for the second time he should proceed to the D.P.M. in 1948 and to restrict his practice to psychiatry.

A fluent linguist, he also retained throughout his life a lasting intimacy with the classical languages of the Indo–Germanic–Celtic stream. In consequence his main interests outside his profession were history and comparative philology.

Those who knew him cherished his company, and by his death they are diminished.

J. M. MOUNSEY, M.B., B.Ch., D.C.H.

Dr. J. M. Mounsey, who served for 26 years as school medical officer and assistant medical officer of health in Portsmouth, died in the Queen Alexandra Hospital, Cosham, on August 13 after a short illness. He was 64 years of age and was due to retire in six weeks' time.

Born in Sheffield, John Milburn Mounsey moved in early childhood to Dublin when his father, an accountant, was transferred there. Educated at the High School and Trinity College, Dublin, where he won a FitzPatrick scholarship, he graduated M.B., B.Ch. in 1923. He then worked for two years at the Dublin Medical Mission, studying tropical

medicine and gaining experience with a view to becoming a medical missionary; unfortunately the illness of his wife prevented his ambition being realized.

A special interest in children's diseases was encouraged by service as house-surgeon at the Royal Alexandra Hospital for Children, Brighton, and the Royal National Orthopaedic Hospital, London, and in 1931 he was appointed school medical officer and assistant medical officer of health, Portsmouth, where he served until his death, except for a period in Northampton and in general practice at Southbourne during the war years. In 1946 he took the diploma in child health.

Possessed of deep religious convictions, Mounsey devoted much of his leisure to church work, while his high moral standards and integrity of character were evident in the scrupulous care he devoted to the examination of the children for whom he was responsible. His advice was often sought by his colleagues, who admired his clinical acumen and held him in great respect. Much sympathy is felt for his widow.—T. E. R.

JULIAN TAYLOR, C.B.E., M.S., F.R.C.S. Hon.F.R.A.C.S.

The obituary of Professor Julian Taylor was published in the *Journal* of April 29 (p. 1255).

Dr. M. A. K. JAVID writes from Iran: May I be allowed a few words about Professor Julian Taylor as one of his old students at University College Hospital? His loss as a great teacher and surgeon is felt all over the world by his many students and admirers. He had special consideration and kindness for his overseas students, who regarded him with great respect and esteem.

R. A. BRYDEN, D.S.O., M.R.C.S., L.R.C.P.

The obituary of Colonel R. A. Bryden was published in the *Journal* of July 29 (p. 316).

Lieutenant-General Sir TREFFRY THOMPSON writes: Having read the obituary notice of Colonel R. A. Bryden I would like to pay a short tribute to his memory. I met him a number of times, both officially and socially, when serving near him in the first world war, and after that war in peace service in India. At that time I thought of him as one of our finest officers. Although strict he was understanding and helpful to all junior officers. He was, later on, one of four or five very good senior officers who were passed over for highest promotion simply because he and the others never drew attention to themselves or advertised themselves. Many of us were amazed and extremely sorry that he had been passed over for further promotion. I still think of him as typical of our best type of R.A.M.C. officer in war or peace, doing a fine job without ostentation.

R. M. GORDON, O.B.E., M.D., Sc.D., F.R.C.P. D.P.H., D.T.M.

The obituary of Professor R. M. Gordon was published in the *Journal* of August 5 (p. 387).

Dr. G. S. W. EVANS writes: Your obituary of Professor R. M. Gordon failed to record the greatest feature of his character, which was courage. As a young battalion medical officer in the first world war, Gordon was much beloved by the officers and men of the 8th South Wales Borderers, for he invariably appeared to succour the wounded at the site of greatest danger and hostility in the front line, when he might well have waited in greater security at his base. His bravery and devotion did much to raise the prestige of the regiment to a very high pitch, and prompted me to state, when he was guest of honour at a recent reunion, that "Professor Gordon was now a very great man, but he never was a greater man than when he was a battalion medical officer on the Salonika front."

Medico-Legal

DETENTION OF CRIMINALS IN MENTAL HOSPITALS

[FROM OUR LEGAL CORRESPONDENT]

Mr. Justice Glyn-Jones, delivering a judgment of the Court of Criminal Appeal on August 15, made certain observations which are likely to have considerable effect upon the practical administration by the courts of the machinery of the Mental Health Act, 1959 (R. v. Higginbotham, *The Times*, August 16).

John Higginbotham (aged 42) was appealing against a sentence of preventive detention imposed on him on his conviction for taking and driving away a motor vehicle without the owner's consent and for dangerous driving. He had a record of 17 convictions between 1931 and 1960. The grounds of Higginbotham's appeal and the reasons for its eventual dismissal by the court need not concern us. What is of importance is the court's reference to the application of the provisions of the Mental Health Act to Higginbotham's case.

In December, 1960, the Hampshire Quarter Sessions made a hospital order in respect of Higginbotham under section 60 of the Mental Health Act, coupled with an order under section 65 restricting the hospital from discharging him without the consent of the Secretary of State. However, on May 13, 1961, he had walked out of the hospital in which he had been received under that order and committed the offences leading to the sentence from which he now appealed.

Commenting on the operation of the Mental Health Act, Mr. Justice Glyn-Jones said that one thing seemed clear: when a hospital order was made the person in respect of whom it was made was received into the hospital not as a criminal but as a patient. A doctor at the hospital receiving Higginbotham examined him and, treating him as a patient, came to the conclusion that there was very little sign of mental illness about him. Accordingly he left him at large to walk about the hospital as he thought fit and to work in the gardens outside, with no physical obstacle to his walking out through the gate at any time he liked. Eventually he had so walked out.

Ensuring Safe Custody

Mr. Justice Glyn-Jones stated that it was unsafe for courts to assume that the making of a hospital order coupled with a restrictive order under section 65 was sufficient by itself to ensure that the convicted person would be kept in custody. The only way to ensure this was for the court to ascertain, before making the order, which mental hospital could receive the man: this must be done. Further, the court must find out whether the hospital had facilities for keeping the patients in safe custody so that they would not have the opportunity to walk out and commit a crime. If there were no such vacancy it should be remembered that the power to make a hospital order was permissive and not mandatory. If the protection of the public demanded that an accused man should be incarcerated (and no vacancy in a secure hospital was available) he should be sentenced to prison in the normal way, leaving it to the prison medical authorities to arrange appropriate medical treatment in some place where the man would be kept in safe custody.

The difficulty of finding places in secure mental hospitals has already been experienced in at least one case by the chairman of the Middlesex Sessions (*Journal*, August 19, p. 527). The effect of these observations falling from the Court of Criminal Appeal will be twofold.

First, there will be an added responsibility upon those preparing a case for trial, since the court will not make a hospital order unless assured that there is a hospital of

appropriate type prepared to receive a prisoner. The Mental Health Act already provides that a hospital order cannot be made unless there is a hospital prepared to receive the prisoner. In many, if not most, cases the court will now also require that hospital to be a secure hospital.

Secondly, the difficulty of finding places in secure hospitals will no doubt result in an increasing number of prisoners being sentenced to prison, although the court would wish them to receive treatment. This will cast a heavy responsibility upon the already overworked prison authorities to make the arrangements which others have failed to make. It is to be hoped that this will not prove too great a burden for them.

Universities and Colleges

UNIVERSITY OF LONDON

Mr. B. N. Catchpole, Reader in Surgery in the University of Adelaide, has been appointed to the University Readership in Surgery tenable at St. Bartholomew's Hospital Medical College.

Mr. J. C. G. Coleridge, Lecturer in the University of Leeds, has been appointed to the University Readership in Physiology, tenable at the Royal Free Hospital School of Medicine.

The following have been appointed, reappointed, or renominated as representatives of the University on the governing bodies of the institutions indicated: *Guy's Hospital Medical School,* Dr. E. R. Cullinan and Dr. J. Forest Smith. *King's College Hospital Medical School,* Professor F. Goldby. *Royal Dental Hospital of London School of Dental Surgery,* Dr. M. I. A. Hunter and Dr. Katharine G. Lloyd Williams. *St. George's Hospital Medical School,* Mr. E. G. Slesinger and Professor J. Z. Young, F.R.S. *Wright-Fleming Institute of St. Mary's Hospital Medical School,* Professor G. Payling Wright. *British Postgraduate Medical Federation,* Sir Francis Fraser and Dr. C. F. Harris. *Royal Masonic Institution for Boys,* Mr. J. B. Hume.

A Ken Clifford Entrance Scholarship in Medicine for 1961 has been awarded to Eileen M. Phillips (City of London School for Girls), and the Sir William Dunn Scholarship for 1961–2 to Thomas Ian Wagstaff (University College).

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on August 3, with Sir Arthur Porritt, President, in the chair, Surgeon Rear-Admiral D. D. Steele-Perkins was admitted to the Fellowship (*ad eundem*).

The Mitchiner Medal for 1961 was presented to Brigadier L. R. S. MacFarlane; the Lady Cade Medal was presented to Wing Commander J. M Urquhart, and the Hallett Prize to Dr. Peter Fells, of the University of Cambridge and University College Hospital; Mr. R. T. Watson, of Marlborough College, was admitted as the thirtieth Macloghlin Scholar; Handcock Prizes were awarded to Jill Bonner Brown, of St. Thomas's Hospital Medical School, and to Nicholas Keith Coni, of Westminster Medical School; and the award of the Sir Gilbert Blane Medal for 1961 to Surgeon Lieutenant-Commander J. H. Sewart, R.N., was reported.

The re-election of Professor M. A. Rushton as Dean and the election of Professor A. B. MacGregor as Vice-Dean of the Faculty of Dental Surgery for the ensuing year were reported.

The readmission to the Board of the Faculty of Dental Surgery of Professor F. C. Wilkinson, Professor R. Cocker, and Mr. A. Shefford, and the admission of Professor G. L. Slack, as representatives of the Fellows in Dental Surgery, and the readmission of Mr. W. Christie Rae to the Board as a representative of the Licentiates in Dental Surgery were reported.

Sir Wilfrid Le Gros Clark, F.R.S., was appointed the Edridge-Green Lecturer for 1961.

A Diploma of Fellowship was granted to Sim-Fook Lam.

Diplomas of Fellowship in the Faculty of Anaesthetists were granted to the following successful candidates:

R. E. Graham, R. B. Roberts, W. D. R. Writer, S. A. Kabir, I. McI. Cochran, Barbara W. Cooke, R. E. C. Gibson, Jean M. Allison, C. J. Friendship, A. S. Gardiner, B. G. Pirie, M. Kaminer, C. G. Lloyd, R. E. Steele, P. O. Bodley, R. McKenzie, G. W. Macnab, Eva R. Seelye, J. M. B. Burn, R. A. Butler, P. Chandra, J. P. Davie, Shu Poh Ma, N. P. Murray, Margaret M. Vovsey, Bridget A. Jepson, S. S. Lutchman, D. C. Maxwell, T. O. G. Ormston, N. J. Paymaster, El T. Fadl, A. Ganendran, G. B. Gillett, A. M. C. Jennings, H. G. Schroeder, J. H. Ll. Bland, A. V. Dreosti, B. Foster, S. M. Hart, D. A. Nightingale, J. F. O'Donnell, B. le G. Waldron.

Diplomas in Laryngology and Otology and in Industrial Health were granted, jointly with the Royal College of Physicians of London, to the successful candidates whose names were printed in the report of the meeting of the Royal College of Physicians of London (August 12, p. 461).

SOCIETY OF APOTHECARIES OF LONDON

The following candidates have been awarded the Diploma in Industrial Health:

S. L. Chadha, G. D. Chetty, D. D. Desai, S. Dobson, J. D. M. Holt, L. J. G. Morgan, W. D. O'Regan, R. Owen, D. A. Slattery.

E. J. R. Rossiter has been awarded the diploma of Mastery in Midwifery.

The following candidates, having completed the final examination, have been granted the diploma of L.M.S.S.A.:

N. K. Coni, S. M. El Dardiry, P. M. J. Ephson, J. D. Fox, G. J. Lumsden, H. Morris, K. C. Ng, P. H. Rees, M. T. S. Roberts, C. C. T. Whaby, G. Van der Wilk, S. S. Woo, D. R. David, F. J. Husain, D. B. D. Jones, I. D. Morrison, T. A. J. Ogunbiyi, E. F. H. Parry, R. K. Saverimuttu, B. P. Krishnamurthy, S. M. Rau.

Vital Statistics

Venereal Diseases

In England and Wales during the quarter ending March 31, 1961, 1,009 new cases of syphilis were reported as attending the clinics, compared with 970 in the previous quarter. Of these, 274 (242 in the corresponding quarter last year) were classified as primary, secondary, or latent in the first year of infection. Seven cases of congenital syphilis in children aged under 1 year were reported and 73 in persons over that age. New cases of gonorrhoea (with corresponding 1960 figures in parentheses) numbered 8,120 (7,291), of chancroid 56 (42), and of non-gonococcal urethritis (males only) 5,280 (4,590).—*Monthly Bulletin of the Ministry of Health,* August, 1961.

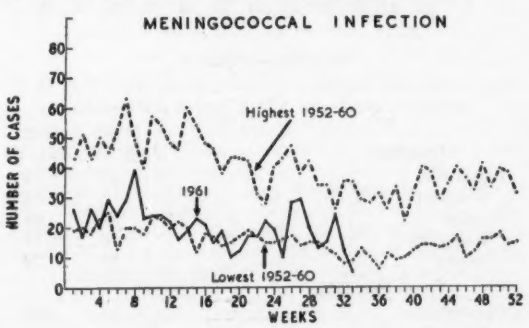
Industrial Accidents and Diseases

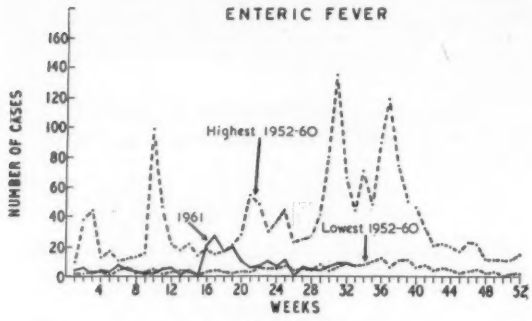
The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in July was 90, compared with 94 in the previous month and 140 in July, 1960.

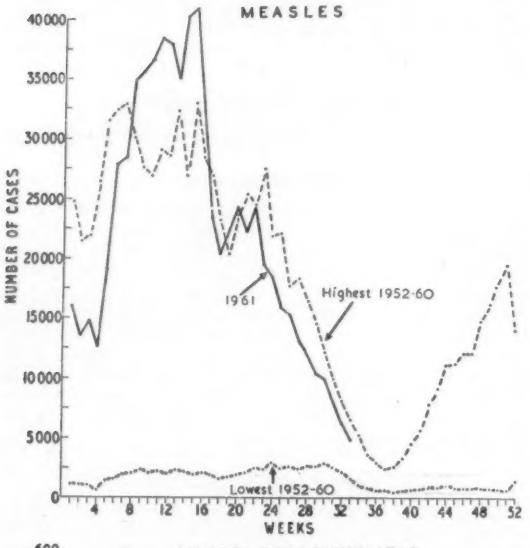
The numbers of cases of industrial diseases in the United Kingdom reported during July were as follows: lead poisoning 4, compressed-air illness 1, epitheliomatous ulceration 19, chrome ulceration 6: total 30. There were two deaths from epitheliomatous ulceration.

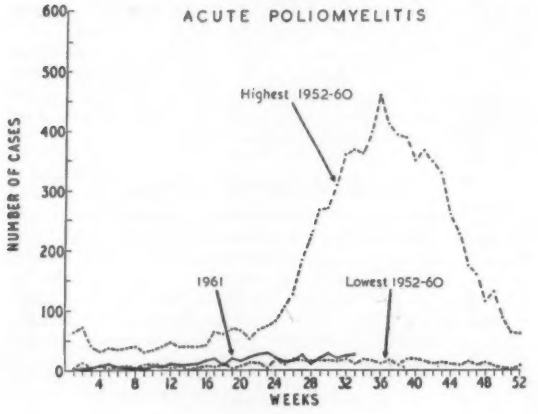
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for 1961 thus ———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending Aug. 19	Aug. 26
Dysentery		
Lancashire	49	**75**
Blackburn C.B.	6	**12**
London	59	**46**
Islington	0	**19**
Glasgow	87	**78**
Food Poisoning		
Lancashire	14	**282**
Blackpool C.B.	0	**253**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 19** (No. 33) and corresponding week 1960.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1961 Eng. & Wales	1961 Lond.	1961 Scot.	1961 N. Ire.	1961 Eire	1960 Eng. & Wales	1960 Lond.	1960 Scot.	1960 N. Ire.	1960 Eire
Diphtheria	0	0	2	0		1	0	0	0	
Dysentery	266	59	152	8	6	346	38	153	12	7
Encephalitis, acute	1	0		0		5	0	0	0	
Enteric fever: Typhoid	4	0	0	0		2	0	0	0	
Paratyphoid	3	0	1 (A) 4 (B)	0		5	2	0	0	
Food-poisoning	144	25	17	4		247	31	23	3	
Infective enteritis or diarrhoea under 2 years				14	22				17	23
Measles*	4,900	92	24	96	55	2,057	114	43	2	2
Meningococcal infection	5	0	9	1		23	0	17	1	
Ophthalmia neonatorum	14	4	2	0		22	4	4	0	
Pneumonia†	127		62	2		139	7	70	1	
Poliomyelitis, acute: Paralytic	19	2	0	0		3	1	1	0	8
Non-paralytic	6	0	1			7	2	2		
Puerperal fever§	185	25	4	1		167	27	8	1	
Scarlet fever	184	14	18	14	6	207	14	24	12	12
Tuberculosis: Respiratory	343	50	44	9		358	47	59	15	
Non-respiratory	67	7	5	1		53	6	9	7	
Whooping-cough	315	12	34	22	8	1,308	87	117	5	16

DEATHS	1961 Eng. & Wales	1961 Lond.	1961 Scot.	1961 N. Ire.	1961 Eire	1960 Eng. & Wales	1960 Lond.	1960 Scot.	1960 N. Ire.	1960 Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0		0	0		0			0
Enteric fever	0	0	0			0	0	0	0	
Infective enteritis or diarrhoea under 2 years	8	0	0	2	0	4	0	2	0	0
Influenza	5	0	0	0	0	3	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	351	26	12	8	1	378	30	13	9	5
Poliomyelitis, acute	1	0		0	0	1	0		0	1
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory	51	4	6	5	2	60	4	1	1	2
Non-respiratory		0		1	0		1	0	0	0
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0–1 year	263	28	25	5	8	278	37	20	2	8
Deaths (excluding stillbirths)	8,401	641	541	86	117	8,622	644	485	96	132
LIVE BIRTHS	16,206	1375	1014	281	395	15,129	1310	969	287	404
STILLBIRTHS	312	19	20			283	25	17		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Feldberg Foundation for German-English Scientific Exchange for Experimental Medical Research

A foundation to endow an Anglo-German lectureship has recently been established by Professor W. FELDBERG, F.R.S., a senior member of the Medical Research Council's scientific staff at the National Institute for Medical Research. Professor Feldberg has set up this foundation out of funds awarded to him by the Federal German authorities as compensation for professional damages. It will be known as the Feldberg Foundation for German-English Scientific Exchange for Experimental Medical Research and will be administered by a board of directors consisting of three German and three British scientists. Each year the board will award a prize to one German and one British research worker of distinction, and in recognition of this gift the German recipient will give a lecture in Britain and the British recipient a lecture in Germany. The prizewinners for 1961 are Sir LINDOR BROWN, F.R.S., Waynflete professor of physiology at the University of Oxford, and Professor Dr. HERBERT HENSEL, director of the Physiological Institute of the University of Marburg. In November Professor Hensel will lecture at University College, London, on "The Electrophysiology of Thermoreceptors," and Sir Lindor Brown will lecture at Heidelberg on "The Adrenergic Neurone." The German Federal Republic has recently conferred a decoration, the "Grosses Verdienstkreuz," on Professor Feldberg in recognition of this endowment.

Medical Research Council

▶ The Medical Research Council's headquarters office will shortly be moving to new accommodation, and from September 18 its address will be 20 Park Crescent, Regent's Park, London W.1 (Telephone: Museum 5422).

▶ The Medical Research Council is to establish a Research Group on Demyelinating Diseases in the University of Durham. The group, to be situated in the William Leech Research Laboratories, Royal Victoria Infirmary, Newcastle upon Tyne, will be under the direction of Dr. E. J. FIELD, senior lecturer in neuropathology, King's College Medical School, and consultant neuropathologist at the Infirmary; Dr. H. G. MILLER, physician in neurology to the Infirmary, will act in an advisory capacity on the clinical side.

▶ Professor M. L. ROSENHEIM, professor of medicine in the University of London at University College Hospital Medical School, and Professor WILSON SMITH, F.R.S., lately professor of bacteriology in the University of London at University College Hospital Medical School, have been appointed members of the Medical Research Council from October 1.

Canadian Medical Research Council

A highlight of the past year has been the establishment of the Medical Research Council (of Canada) as an autonomous body associated with the National Research Council, says the N.R.C.'s *Forty-fourth Annual Report*. In the Medical Research Council's section of the report, its chairman, Dr. R. F. FARQUHARSON, describes how in the past money has been made available for research. In 1938 the first Associate Committee on Medical Research of the N.R.C. had a budget of $53,000. After the war a Division of Medical Research was established with an initial budget of about $200,000; this was increased to $900,000 by 1957, and in the last three years to $2,300,000. After the war various Government departments assisted medical research relevant to their own interests, and by 1959–60 total Government support for extramural research had risen to $5m.; voluntary foundations and organizations provided an additional $2m. During the year under review the Canadian M.R.C. has supported all fields of medical research with particular emphasis on biochemistry and physiology. Fundamental studies on the nature of disease, studies in experimental surgery, and various aspects of morphology particularly in the field of ultrastructure were also supported.

Chair of Paediatrics, University of Hong Kong

Dr. C. ELAINE FIELD, temporary consultant paediatrician to the South Manchester Group of Hospitals, has been appointed to the chair of paediatrics in the University of Hong Kong.

Dr. Field, who is 50, studied at University College and University College Hospital, London. She qualified M.B., B.S. in 1934, proceeding M.D. in 1937, and she took the M.R.C.P. in 1941. She held various junior and registrar appointments before being appointed first assistant to the Children's Department, University College Hospital, London. During the war she worked in the Emergency Medical Service, mainly in the base hospitals for the Hospital for Sick Children, Great Ormond Street, and U.C.H. After the war she was granted a Nuffield Fellowship in Child Health and spent a year in the U.S.A., mainly at the Boston Children's Hospital and as Research Fellow in Paediatrics at Harvard College, Boston. She also travelled in Scandinavia and Finland. In 1948 she was appointed assistant to the director at the Institute of Child Health, London. She went to Malaya in 1949 as child health specialist, Federation of Malaya, transferring in 1955 to Singapore as senior paediatric specialist at the General Hospital and part-time lecturer in the University of Malaya. In 1959 she was elected Master of the Academy of Medicine at Singapore. Dr. Field's research has been chiefly concerned with the clinical study of bronchiectasis.

First Congolese Doctor

Dr. MARCEL TSHIBAMBA is one of the two citizens of the Congo who have recently graduated from the medical faculty of the University of Lovanium near Leopoldville, the first ever to do so. Before he graduated he had been made Commissioner-General of Health for the Congo, and was a member of the cabinet of students set up by Colonel MBOTU temporarily to run the affairs of the country.

[W.H.O. Photos

Dr. Tshibamba was born in 1931, the fifth child of a poor cultivator and the only one to be educated. He started school at 10 in his village, went on to Luluabourg, and then to a Catholic mission at Kabwe before spending two years at one of the Congo's training colleges for medical assistants. In 1954, when the medical faculty of the new University of Lovanium was opened, he was one of the first five Africans to be admitted; two completed the course. By 1965 18 doctors should have qualified and the World Health Organization has provided additional professors at Lovanium so that more medical students can be admitted. Seven Congolese are studying medicine in Europe on W.H.O. Fellowships, and 60 medical assistants are being given additional medical training in France.

Nuffield Orthopaedic Centre's Research House

A research house is to be presented to the Nuffield Orthopaedic Centre, Oxford as an extension of the existing Disabled Living Research Unit. The house is the gift of Lady HAMILTON, a member of the Executive of the Central Council for the Care of Cripples, which is sponsoring the scheme. It will be built on a site adjoining the Mary Marlborough Lodge at the Centre, and will be lived in by disabled patients and their families during the final phase of their rehabilitation. It is hoped that the design of house and equipment which will be evolved after full testing will be used and adapted by local authorities and private builders concerned with housing the disabled.

"Biochemistry"

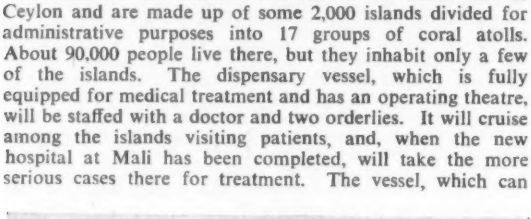
Biochemistry, a new bi-monthly journal, is to be published by the American Chemical Society in January next year. It will concentrate on original research in all areas of fundamental biochemistry, and will emphasize the relationship between chemistry, biochemistry, and the other biological sciences. The editor is Dr. HANS NEURATH, chairman of the biochemistry department of the University of Washington, Seattle. The subscription to non-members of the A.C.S. will be $26 a year, and inquiries should be sent to the Society at 1155 Sixteenth Street, N.W., Washington 6, D.C., U.S.A.

In Brief

A hospital for retarded children has been built at Cedar Springs on behalf of the Ministry of Health, Ontario, Canada, at a cost of £4,630,000. It will have 1,200 beds, and will provide hospital and residential facilities, rehabilitation, and school and vocational training.

Dispensary Vessel for Maldive Islands

A dispensary vessel, *Golden Ray*, has recently been built and equipped for service in the Maldive Islands. It is one of the projects planned by the United Kingdom Government in return for certain territorial concessions on Gan Island. The Maldives lie about 400 miles to the south-west of Ceylon and are made up of some 2,000 islands divided for administrative purposes into 17 groups of coral atolls. About 90,000 people live there, but they inhabit only a few of the islands. The dispensary vessel, which is fully equipped for medical treatment and has an operating theatre, will be staffed with a doctor and two orderlies. It will cruise among the islands visiting patients, and, when the new hospital at Mali has been completed, will take the more serious cases there for treatment. The vessel, which can



The dispensary vessel *Golden Ray*.

reach a speed of 11 knots and whose length is 75 feet, beam 18 feet, and draught about 6 feet 3 inches, was built in the Singapore yard of John I. Thornycroft and Co. Ltd.

People in the News

▶ Sir JOHN COCKCROFT, O.M., F.R.S., has been elected president for next year of the British Association for the Advancement of Science.

▶ Lord COHEN OF BIRKENHEAD, president of the National Society for Clean Air, has been appointed a member of the Clean Air Council.

▶ Miss IDA MANN, consultant in ophthalmology to the Government of Western Australia, was elected vice-chairman of the World Health Organization's third Expert Committee on Trachoma, which met recently in Geneva.

▶ Dr. W. D. BUCHANAN, H.M. Deputy Senior Medical Inspector of Factories, is to be a member of the reappointed Joint Standing Committees on Health, Safety, and Welfare in Non-ferrous Foundries, and in Steel Foundries.

▶ Sir WILFRID LE GROS CLARK, F.R.S., and Professor E. J. KING, D.Sc., were among the 25 people who received honorary doctorates during Oslo University's 150th anniversary celebrations.

COMING EVENTS

Birmingham Medical Institute (Section of Psychiatry).—Annual dinner, October 9, 7.30 p.m., Board Room, Queen Elizabeth Hospital. Guest of honour: Professor P. C. P. CLOAKE. Applications for tickets (25s. each) to Secretary, Birmingham Medical Institute, 36 Harborne Road, Birmingham 15, by September 18.

2nd British Congress on History of Medicine and Pharmacy.—London, September 27–29, "Chemistry in the Service of Medicine." Details from Dr. F. N. L. POYNTER, Wellcome Historical Medical Library, Wellcome Building, Euston Road, London N.W.1.

Family Planning Association.—Training courses for medical practitioners, London, Manchester, Birmingham. Details from F.P.A., 64 Sloane Street, London S.W.1.

R.A.F. Medical Branch.—Annual dinner, October 13, Royal College of Surgeons of England. Details from Air Ministry (M.A.3), 1–6 Tavistock Square, London W.C.1.

Faculty of Radiologists.—Edinburgh meeting, October 14. Details from Faculty, 47 Lincoln's Inn Fields, London W.C.2.

Congress of Industrial Medicine.—Berlin, October 19–21. Details from Deutsche Gesellschaft für Arbeitsschutz e.V., 1–3 Schumannstrasse, Frankfurt-am-Main 16, Germany.

International Congress of Scientific, Medical, and Health Documentary Films.—Pavia, Italy, October 22–29. Details from Centro Culturale Cinematografico Italiano, 31 Via Dalmazia, Rome, Italy.

Society for Psychosomatic Research.—Conference, "The Role of Psychosomatic Disorder in Adult Life," November 3 and 4, Royal College of Physicians, London S.W.1. Attendance by invitation. Applications to Hon. Secretary, Dr. H. H. WOLFF, 70 Harley Street, London W.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, September 15

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. R. Bignall: clinical demonstration.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Fallon.—On August 31, 1961, at Glasgow Royal Maternity Hospital, to Valerie and Ronald Fallon, M.D., a third daughter—Alison Wendy.

Hall Hall.—On July 21, 1961, to Mary (formerly Whittaker) and Dr. Francis Hall Hall, of Funtington Down, near Chichester, Sussex, a daughter—Jennifer Jane.

Scott.—On August 23, 1961, at Leeds Maternity Hospital, to Drs. Mary Helena (formerly Davies) and Jack Scott, a brother for Jane—David Neil.

Zoob.—On August 25, 1961, at Kingsbury Maternity Hospital, London N.W., to Greta (formerly Mottelson) and Dr. Max Zoob, a second son—David Simon.

DEATHS

Beattie.—On August 13, 1961, William Forbes Beattie, M.B., Ch.B., Surgeon Captain, R.N., retired.

Bourke.—On August 11, 1961, at Hythe, Southampton, Una Doris Bourke, M.B., B.S., D.P.H.

Brohier.—On August 9, 1961, in Ceylon, Eric Stanley Brohier, L.R.C.P.&S., L.R.F.P.S., late of Ceylon Medical Service.

Burne.—On Augus 15, 1961, at Hove, Sussex, Patricia Burne, M.B., B.S., D.Obst.R.C.O.G.

Campbell.—On August 9, 1961, at 111 Mill Lane, Liverpool, Alexander Fraser Campbell, M.B., Ch.B., D.P.H.

Chauncey.—At Lagos, Nigeria, on August 9, 1961, Antoni Chauncey, M.B., Ch.B., aged 45.

Cohen-Andre.—On August 15, 1961, in St. Mary's Hospital, London W., Werner Cohen-Andre, M.D., of 8 Litchfield Way, London N.W., aged 60.

Cumming.—On August 3, 1961, at Liverpool, Arthur William Gordon Cumming, M.B., Ch.B.

Davidson.—On August 7, 1961, Sonny Sneir Davidson, M.R.C.S., L.R.C.P., of 25 Broadlands Road, London N.

Davie.—On August 7, 1961, at St. Helen's Lodge, Chesterfield, James Paterson Davie, M.D.

De Mirimonde.—On August 3, 1961, at 76 Castlegate, Malton, Yorks, Henry Oscar Pomme De Mirimonde, L.R.C.P.&S.Ed., L.R.F.P.S., aged 90.

Galsworthy.—On August 6, 1961, at St. Albans City Hospital, Beatrice Clara Galsworthy, M.B., Ch.B., of 14 Marford Road, Wheathampstead, aged 88.

Hammerton.—On August 4, 1961, at 57 Esplanade, Hornsea, Yorks, George Herbert Leonard, C.M.G., D.S.O., L.R.C.P.&S., L.R.F.P.S., Colonel, R.A.M.C., retired.

Hudd.—On June 21, 1961, at Launceston, Tasmania, Harry Ronald Hudd, M.B., B.Ch.

Kay.—On August 13, 1961, Gordon Kay, L.R.C.P.&S., of Westfield, Moorends, Doncaster.

Lafferty.—On August 5, 1961, Gerald Patrick Lafferty, M.B., B.Ch., of Edale, Sheffield, aged 63.

Leach.—On August 1, 1961, at Northampton, Herbert Leach, M.R.C.S., L.R.C.P., late of Northern Rhodesia and Isle of Man, aged 85.

Michael.—On July 27, 1961, at Coleraine Hospital, Northern Ireland, William Michael, M.B., B.Ch., B.A.O.

Michaelis.—On August 8, 1961, Willy Michaelis, M.D., aged 75.

Mounsey.—On August 13, 1961, John Milburn Mounsey, M.B., B.Ch., D.C.H.

Pairman.—On July 30, 1961, in Christchurch, New Zealand, James Carmichael Pairman, M.B., Ch.B.

Paterson.—On August 7, 1961, at Eildon Street, Edinburgh, Frank Salmon Paterson, M.B., Ch.B., D.T.M.

Phipps.—On August 10, 1961, at 317 Hills Road, Cambridge, Geoffrey Phipps, M.B., B.S., aged 52.

Spicer.—On August 13, 1961, at Leven House, Westbourne, Bournemouth, Harry Spicer, M.B., Surgeon-Commander, R.N., retired.

Zimbler.—On August 9, 1961, in Middlesex Hospital, London W., Abram Ber Zimbler, M.R.C.S., L.R.C.P.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Tuberculosis in the Factory: Employer's Liability

Q.—*A manufacturing firm is thinking of employing some ex-Service men who have had tuberculosis but are now said to be free from the disease. What would be the legal position should the firm employ these men and some of the present healthy employees develop tuberculosis and claim that they caught the infection as a result of contact with the new recruits?*

A.—An employer has to take reasonable care for his workpeople's safety so as not to expose them to an unnecessary risk. Unless the medical evidence is definite that there is no risk of contracting the disease from daily contact with a number of the new recruits in the confines of a factory, the plan has obvious dangers. To be entitled to damages, any one of the present employees who contracted the disease would have to show that he had caught the infection from the new recruits. Although strict proof would be impossible, a strong enough inference to convince a jury might be raised by a plaintiff working alongside men careless, perhaps, in their personal habits. Because of widespread ignorance and prejudice concerning tuberculosis, the present workpeople would probably have to be asked their views before the plan was put into effect. That a plaintiff had consented would be a complete defence to a claim for damages. Consent is unlikely to be unanimous, and the effect on labour relations of introducing a plan despite objections is a wider question which I am not asked to answer.

Malaria Prophylaxis

Q.—*What malaria prophylactic should be taken by a person who is going to work in Ghana?*

A.—Several prophylactics are available and all are highly effective if properly used. Proguanil (" paludrine ") combines greatest efficacy with least toxicity, and may be given in doses of 100 mg. daily, beginning on the day of entering the malarial area and continuing until the individual has been away from it for two weeks. Some recommend that this amount should be doubled for those living in particularly malarial regions.

Pyrimethamine (" daraprim ") in doses of 25 mg. weekly and chloroquine in doses of 300 mg. (base) weekly have the advantage of less frequent administration. But there are advantages in using malarial prophylactics daily, for when a weekly dose is forgotten the individual may not take a prophylactic for a fortnight—i.e., he will go for longer than the incubation period of malaria without taking the prophylactic. Daraprim is tasteless and therefore easy to administer to children. However, several tragedies have occurred as a result of children taking the tablets instead of sweets, and it is important to guard against this possibility.

Constitutional Precocity

Q.—*A girl aged 10 has had a tender unilateral uniform swelling of the breast for three months. Is there any significance in this, and should it be treated?*

A.—Since the question does not mention any secondary signs of sexual development, such as growth of pubic hair, etc., it may be taken that these are absent, and also that the girl is normal for her age in height, weight, and general development. Under these circumstances it is unlikely that the condition is due to any of the well-recognized gonadal dysplasias, or rare other lesions, which lead to pathogenic precocity. It seems, therefore, that this case falls into the category sometimes called constitutional or the genetic type of precocity. The fact that the condition is at present unilateral is no objection to this diagnosis—provided of course that any local lesion of the breast or its suroundings has been excluded. Although due to a general hormonal adjustment, for some unknown reason one breast is often affected long before the other, as indeed happens even more frequently in the corresponding male condition of pubertal gynaecomastia. It would probably be wise to wait for a longer period before subjecting the patient to further investigations such as urinary estimations of ketosteroids, hormones, and so on.

Immunization Programme Preparatory to Visiting India

Q.—*A patient travelling to India in five months' time for a prolonged stay wishes to be immunized against typhoid (including the paratyphoids), cholera, and tetanus. What would be the most satisfactory scheme for carrying this out in the time available?*

A.—This patient could be inoculated against typhoid, paratyphoid, cholera, and tetanus very easily in a matter of a few weeks. However, since he has had the good sense to make inquiries five months in advance of his date of departure, there is ample time to space out the administration of the three vaccines—always a desirable procedure in immunization. The first vaccine should be typhoid–paratyphoid A and B and tetanus vaccine (T.A.B.T./Vac)—the first dose immediately, the second four to six weeks later, and the third just before departure. The interval between the second and third doses should normally be at least six months, but, although in this case the interval will be only three and a half months, the third dose will have a useful effect in reinforcing the first and second doses. A fourth dose should be given one year or so after he reaches India, in order to reinforce protection. Immunization against cholera can conveniently be accomplished by giving two injections of cholera vaccine (Cho/Vac). Since the protection afforded against cholera lasts for only about six months, the vaccine should be given as near as possible to the time of departure. Assuming a period of 20 weeks before departure, I would suggest the following schedule:

Week 1.—T.A.B.T./Vac. (1st injection).
Interval of four weeks.
Week 5.—T.A.B.T./Vac (2nd injection).
Interval of eight weeks.
Week 13.—Cholera vaccine (1st injection).
Interval of four weeks.
Week 17.—Cholera vaccine (2nd injection).
Interval of one week.
Week 18.—T.A.B.T./Vac (3rd injection).

This leaves one to two weeks before departure, allowing the traveller time to get over the third T.A.B.T./Vac and to complete his transport arrangements.

It is presumed that the traveller has been vaccinated or revaccinated against smallpox and yellow fever, otherwise these would have to be fitted into the schedule—possibly between weeks 5 and 13. If he has not been vaccinated against smallpox before (or since infancy), three weeks should separate smallpox vaccination from any other immunological procedure.

Vitamin E in Mongolism

Q.—*Is there any evidence that vitamin E is of value at any stage of mongolism?*

A.—There is no evidence that vitamin E is of any value at any stage of mongolism. Mongolism is now thought, in most cases, to be due to non-dysjunction of chromosomes during ovulation in the patient's mother, or occasionally in a previous generation. It is not known what factors cause this non-dysjunction, but it seems possible that these are hormonal. No definite class distribution has been

demonstrated in mongolism, as would be expected if there were any question of vitamin deficiency in the aetiology. Once the defect of mongolism is established, there is no known treatment which will ameliorate the condition after birth. Indeed, the nature of the metabolic error is not known with certainty. Sobel *et al.* suggested[1] that children with mongolism have lowered capacity for absorption of vitamin A, whilst Gershoff and his colleagues[2 3] found anomalies in vitamin-B metabolism. The subject is full of pitfalls and needs careful reinvestigation before any practical recommendation can be made.

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1 Sobel, A. E., Strazzulla, M., Sherman, B. S., Elkan, B., Morgenstern, S. W., Marius, N., and Meisel, A., *Amer. J. ment. Defic.*, 1958, **62**, 642.
2 Gershoff, S. N., Hegsted, D. M., and Trulson, M. F., *Amer. J. clin. Nutr.*, 1958, **6**, 526.
3 —— Mayer, A. L., and Kulczycki, L. L., ibid., 1959, **7**, 76.

Daily Fluoride

Q.—*From an answer to a previous question,[1] we learn that 1 mg. of fluoride daily supplementary to that in foods is optimal to prevent dental caries. Would it be advisable to give this in a daily pill until such time as fluoride is added to drinking-water or cooking-salt? How is fluoride dispensed in tablets?*

A.—The regular ingestion of tablets containing appropriate amounts of fluoride has often been advocated as a means of controlling dental caries in low-fluoride areas, but until recently there was little substantial evidence to show their effects.[2–6] Wrzodek[6] showed an average reduction of 20% in the incidence of caries in over 13,000 schoolchildren who had been given fluoride tablets over a four-year period, compared with a control group of 4,000 children. Arnold, McClure, and White[7] administered tablets to 131 children whose parents were physicians, dentists, or employees of the United States public health service, and showed (1) that the eventual incidence of caries in them was comparable with that of children of similar ages who drank water containing 1 p.p.m. of fluoride; (2) that the mean fluoride content of their deciduous teeth was significantly higher than the mean content of deciduous teeth of children in a non-fluoride area; and (3) that the ingestion did not result in dental fluorosis of any cosmetic significance. It is noteworthy that in this investigation nearly two-thirds of the children began to take their fluoride tablets before their third birthday, and almost all before their sixth birthday. For the children aged under 2 years one fluoride tablet containing 2.2 mg. sodium fluoride was dissolved in one quart (1.1 litres) of water, which was given for drinking, including the preparation of the babies' bottles, etc. (This is a higher dosage than would be generally advocated in this country.) One tablet was administered directly or dissolved in water, milk, or fruit juices to the children aged 2–3 on alternate days and daily to the children aged 3–10. In every case before administration the fluoride content of the local water supply was analysed to confirm that it had a low fluoride content.

This method of fluoride administration can be recommended, in areas with water supplies containing under 0.3 p.p.m. of fluoride, for children of responsible and educated parents and for pregnant women who will carry out the regimen conscientiously and exactly. But, as stated by Arnold *et al.*, water fluoridation remains a more practical and more dependable procedure for controlling caries in large population groups. Suitable tablets containing 2.2 mg. sodium fluoride in a sodium chloride base are obtainable. Tablets containing the fluoride in the form of calcium fluoride have been advocated, but there is less evidence for their beneficial effects on the incidence of caries.

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4 Bibby, B. G., Wilkins, E., and Witol, E., *Oral Surg.*, 1955, **8**, 213.
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NOTES AND COMMENTS

Typewriting and Haemophiliacs.—Dr. F. NOUR-ELDIN (Bristol) writes: With reference to the question dealing with this subject ("Any Questions?" July 22, p. 257) may I be allowed to mention the following? My experience with 268 cases of haemophilia and Christmas disease shows that only 192 patients suffered from spontaneous haemarthrosis. Among these the incidence of interphalangeal bleeding was low, about 3%. Rapid and frequent movements of the interphalangeal joints do not seem to precipitate attacks of haemarthrosis whether or not the patient has a high level of Bridge anticoagulant.[1] Thus I have on several occasions recommended young haemophiliacs to learn typing, which has proved helpful in their limited field of employment. Also the manipulation of a telephone switchboard is considered safe. Only those with severely affected wrists (less than 6%) are unable to pursue these occupations satisfactorily. Furthermore, since many patients have to restrict their social activities, playing the piano, in my opinion, is a useful hobby which could be encouraged in suitable patients. However, since the elbows are involved in about 50% of the patients, this may not be feasible. I was very pleased to see a haemophilic boy, in spite of his having spontaneous bleeding episodes and a paralysed right upper limb (as a result of poliomyelitis in childhood), managing under careful instruction to use his left hand for learning typing and pianoforte. Eventually he was actually able to play quite successfully simple melodies (for one hand) for charitable purposes. Already affected joints did not hinder another patient from having organ lessons. Nevertheless, reasonable freedom of the joints is necessary for progressive playing of this instrument. The only objection to typing I have met is that these young male patients look upon secretarial work as being an occupation for the fairer sex.

REFERENCE

1 Nour-Eldin, F., *Lancet*, 1961, **1**, 1233.

Vaginitis in a Child.—Mr. G. F. LANGLEY (Ipswich) writes: In your interesting reply regarding treatment for a slight vaginal discharge since babyhood in a healthy child aged 4½ ("Any Questions?" May 13, p. 1405) I note no mention of the possibility of an ectopic ureter in association with a duplex kidney, or even a malpositioned kidney. I have had the opportunity of investigating and treating three children since 1945 in whom a diagnosis of vaginitis had been made associated with bed-wetting occasionally at night or commonly with vaginal discharge and urinary incontinence in the daytime in spite of normal voiding of urine. It might first be advantageous to submit the young girl to investigation by an intravenous pyelography, or probably administration of indigo carmine accompanied by the insertion of a minute vaginal gauze pack to ascertain whether coloured urine is excreted direct into the vagina. Treatment is, of course, surgical if the condition is found to be associated with an ectopic ureter.

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